Interpretation of weak D types in female patients of child-bearing potential – are UK transfusion laboratories making the correct decisions? Evidence from a UK NEQAS (BTLP) exercise

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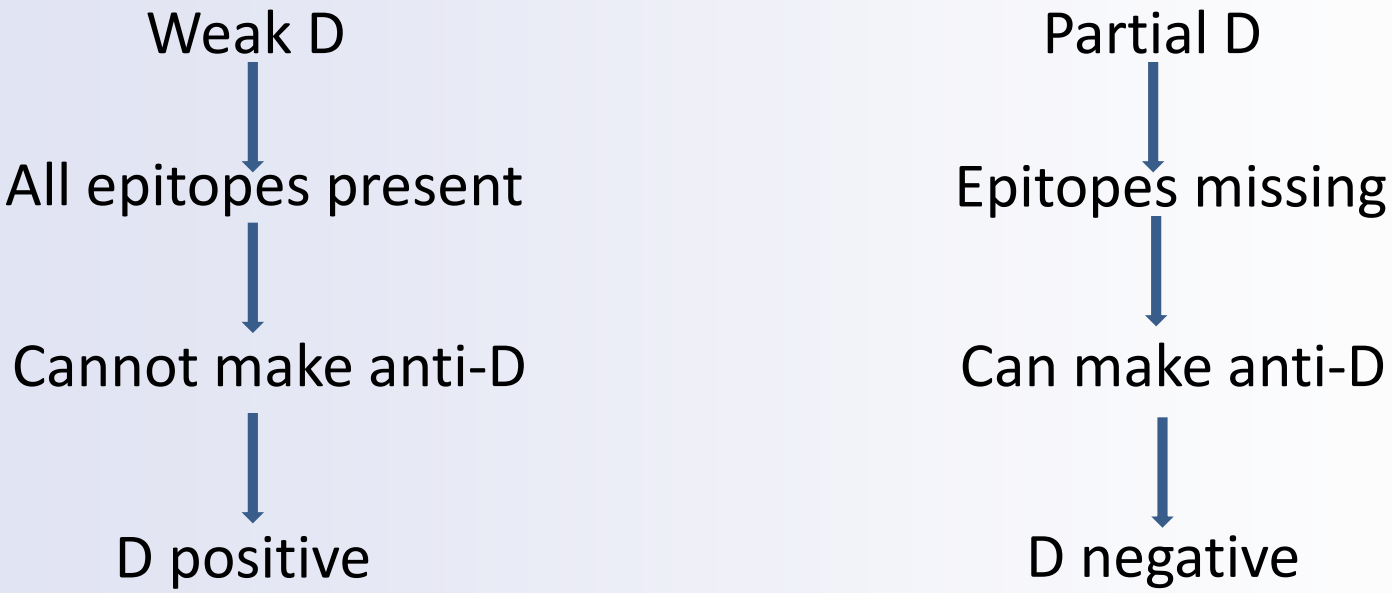
UK NEQAS

The good old days...



Still a problem for hospitals as weak and partial D could not be distinguished by routine testing

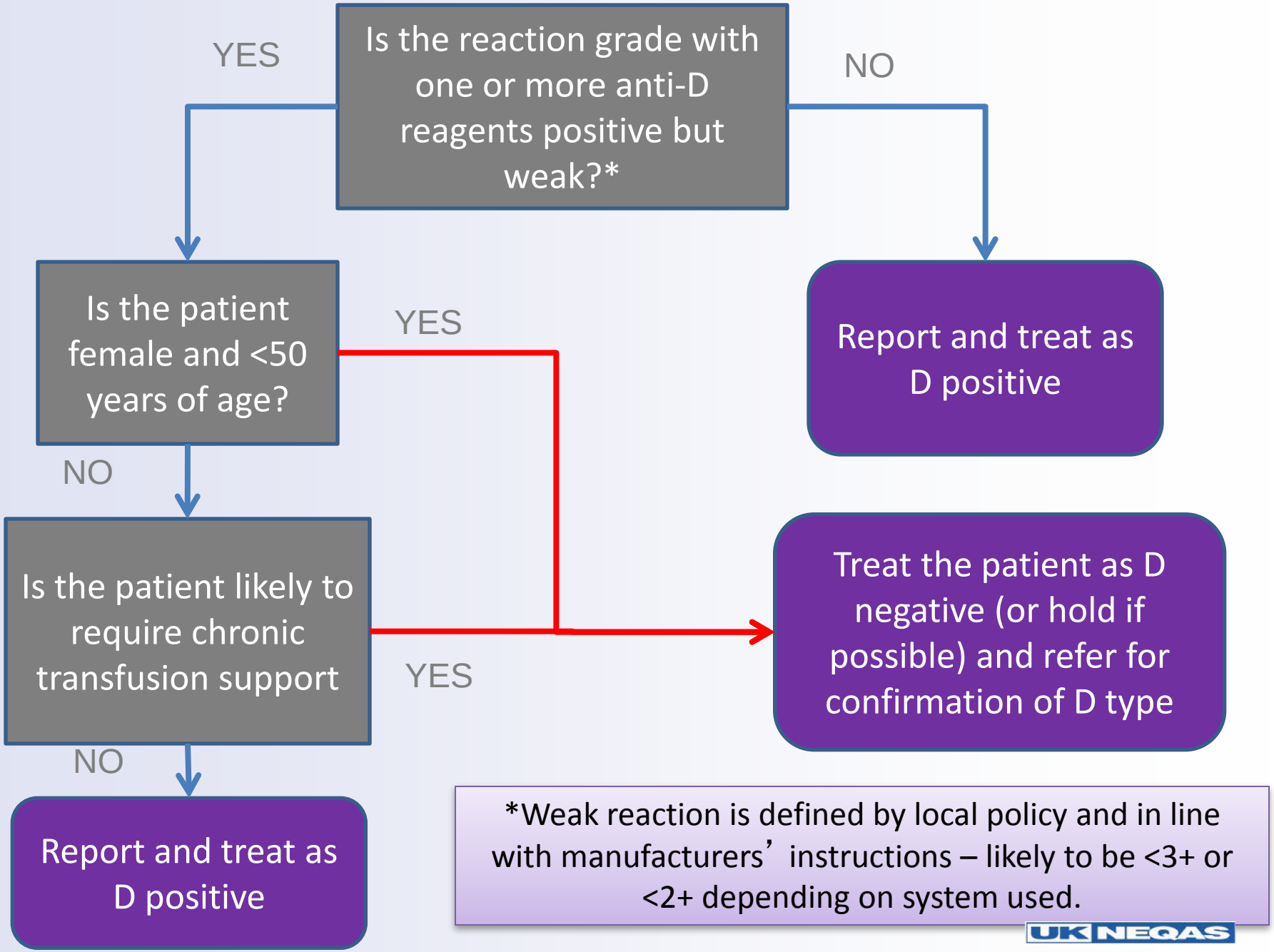
‘Weak’ D individuals have made anti-D; e.g. Types 4.2 and 15

How to define weak and partial D?

Serological or molecular testing?

Historical distinction between weak and partial D has become blurred and a new algorithm is included in the 2013 pre-transfusion testing guidelines

Suggestion of a single term of D variant
Daniels G, Poole G, Poole J, *Transfusion Medicine*, 2007, **17**, 145 146


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.

Which D variants cannot make anti-D?

- Weak D types 1, 2 and 3 (˜93%) rarely, if ever, make allo anti-D and can be regarded as D positive:
  - Types 1 and 2 (˜ 88%) can be identified with an extended D typing panel
  - Type 3 requires molecular testing
- Treat the rest as D negative

- Daniels G (2013)

UK NEQAS 14R1 January 2014

- D typing for a D weak patient and result interpretation in context of age and gender (Patient 1: female, aged 30)
- Transfusion of D positive red cells
- Short survey collecting details of ABO/D typing relating to 14R1 to establish any link between anti-D reagent and D typing result for the weak D
- Sent to 400 clinical laboratories in UK and Republic of Ireland
  - 394 results analysed (4 non return, one unable to test, one not registered for D typing)

Summary of material

- Patient 1 - Group O D weak, inert (female, age 30, not transfusion dependent)
  - *Prepared from a pool of (uncategorised) weak D donations*
- Donor W - O D positive R_1R_1 (CDe/CDe), K-

D typing: Reaction grades recorded

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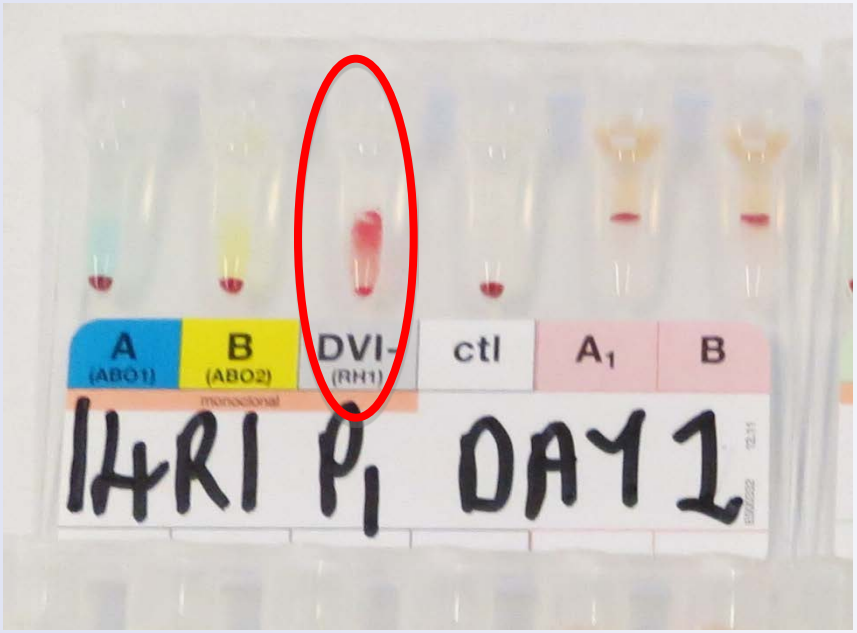
Interpretation (number)	Combination of reactions recorded with anti-D reagent(s)			
	Includes a weak pos[1]	Includes MF	Strong pos only[1]	Neg only[1]
D Variant (191)				
D Positive (121)				
D UI [2] (66)				
D Negative (16)				
Total (394)	293	63	24	14

[1] With one or two anti-D reagents
[2] Unable to interpret

356/394 (90%) recorded anomalous reactions with one or more than one anti-D reagent

In-house ABO/D typing results



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D typing: Reaction grades and interpretations recorded

Interpretation (number)	Combination of reactions recorded with anti-D reagent(s)			
	Includes a weak pos[1]	Includes MF	Strong pos only[1]	Neg only[1]
D Variant (191)			0	1
D Positive (121)			24	0
D UI [2] (66)			0	0
D Negative (16)			0	13
Total (394)	293	63	24	14

[1] With one or two anti-D reagents
[2] Unable to interpret

D typing: Reaction grades and interpretations recorded

Interpretation (number)	Combination of reactions recorded with anti-D reagent(s)			
	Includes a weak pos[1]	Includes MF	Strong pos only[1]	Neg only[1]
D Variant [3] (191)	177	13	0	1
D Positive (121)	94	3	24	0
D UI (66)	21	45	0	0
D Negative (16)	1	2	0	13
Total (394)	293	63	24	14

[1] With one or two anti-D reagents
[2] Unable to interpret
[3] Weak or partial

97/394 (25%) reported D positive based on anomalous D typing reactions = 27% of the 356 recording anomalous reactions

4/86 (5%) stated that they used an extended partial D typing kit

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D typing techniques used 14R1

ABO/D technology	No. UK Labs
DiaMed	184 (52%)
BioVue	101 (29%)
Liquid phase microplate	37 (10%)
Tube	22 (6%)
Grifols	10 (6%)
Total	354 (100%)

90% return rate on accompanying questionnaire

Most common configuration of reagents

* No. Using this as a single test for P1

Manufacturer and configuration	Clones	No.	No*	Str	Wk	MF	Neg
BioVue							
ABORh Combo(A B D Ctrl rev rev)	D7B8	82	46	2	19	25	0
ABODD (A B AB D D Ctrl)	D7B8 + RUM-1	15	9	1	5	3	0
DiaMed							
ABO/D Rev (A B D Ctrl rev rev)	LDM3 + 175-2	126	95	14	79	1	1
ABO/D Rev (A B D D rev rev)	5 clones	44	32	4	23	5	0
LPM - Immucor							
Immuclone & Novoclone	RUM-1 + D175+D415	33	12	0	7	0	5
Grifols							
A B D D Ctrl N N (+ K or N)	P3x61 + MS-201	9	8	0	8	0	0
Tube							
Various	RUM-1 + BS-201	14	9	1	6	1	1

Selection of red cells

Interpretation P1 D type (number)	Result for Donor W (D positive) vs. Patient 1 (weak D)	
	Compatible – Would transfuse	Would not select/transfuse
D Variant (189)	71	118
D Positive (118)	108	10
D UI (65)	14	51
D Negative (16)	3	13
Total (388)	196	192

88/196 (45%) issuing the D positive unit reported D variant, D UI or D neg

7/88 (8%) said that they used an extended partial D typing kit

81/270 (30%) who made an interpretation other than D positive, would have transfused the D positive unit without knowing the variant subtype

Summary

- Variation in reaction grades even with same reagents and techniques
- 27% made an interpretation of D positive following anomalous D typing results (only 4 used an extended D typing kit)
- 30% of those who reported an anomalous D type, stated that they would have issued the D positive donation

Limitations

- EQA exercise
- Patient demographics not usually supplied
  - May not have been taken into account by all
- Some may have ticked the wrong box for ‘would you issue the unit?’
- ? No excuse for interpreting an anomalous results as D positive even if the patient details are not available.

Conclusion

UK NEQAS data suggests that up to 30% of clinical 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

References

1. Daniels G, Poole G, Poole J. (2007) Partial and weak D; can they be distinguished? *Transfusion Medicine*, **17**, 145-146
2. Daniels G. (2013) Variants of RhD - current testing and clinical consequences. *BJH*, **161**, issue 4, 461-470
3. BCSH guidelines for pre-transfusion compatibility testing in blood transfusion laboratories. Transfusion Medicine volume 23, issue 1, pages 3-35 February 2013, and at www.bcshguidelines.com (accessed 11/02/14).