NHS
Blood and Transplant

Genotypes, phenotypes and matching - how much is enough?

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Caring Expert Quality

Selecting blood for transfusion

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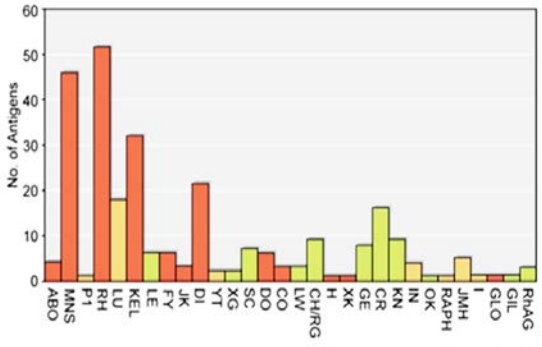
- 300 inherited antigens (blood groups)
- <50 polymorphic
- Not all problematic for transfusion



After Anstee 2009

Commonly	Uncommon and significant	Uncommon and rarely significant
ABO	Di	Lu
Rh	Do	Yt
MNS	Co	In
Kell	H	JMH
Fy	Glo	
Jk	Many other rares	

Mandatory matching-ABO

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7.7.1. Red cell components of the same ABO group as the patient should be selected whenever possible.

7.7.2. If ABO identical blood is not available for group A or B patients, group O blood should be used, and provided it is in additive solution, it does not need to be tested for high titre haemagglutinins as the volume of residual plasma is too small to cause haemolysis (AABB, 2011).

7.7.3. Group AB should be used for AB patients, but if unavailable, group A or B red cells should be selected rather than group O.

7.7.4. Group O red cells should be used in the following situations where transfusion cannot await full investigation and resolution because transfusion is deemed clinically urgent….:

Mandatory matching D

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7.8.1. Selection of D matched blood is the recommended best practice, and D positive blood should be selected for D positive patients according to the definition in the flowchart. However, in order to preserve supplies of D negative red cells for D negative women of child bearing potential, D positive red cells maybe selected for D negative patients in the following situations:

i. Female patients > 50years.

ii. Adult males who are D negative or whose D status is unknown.

iii. Patients undergoing a large volume transfusion (> 8 units), excluding children, females of childbearing potential and patients with immune anti-D.

Mandatory matching – alloantibody

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7.10.1. Red cells should be selected which have been phenotyped and found negative for the relevant antigen. It is good practice to give K negative red cells to these patients because it is sometimes difficult to exclude anti-K in the presence of other antibodies and easy to select K negative units.

7.10.2. Antigen negative red cells should also be selected when a clinically significant antibody has previously been identified, but cannot be detected or identified in the current sample.

7.10.3. Patients with anti-D who are rr (ccddee) should receive rr (D- C- E-), K negative blood.

7.10.4. Patients with other Rh antibodies should be additionally matched for C, c, E and e in order to prevent further Rh alloimmunisation, provided this does not impede delivery of effective transfusion support.

Beyond the mandatory – benefits

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Reducing the risk of transfusion reactions due to undetectable antibodies

- in the current sample
- in future samples

Increasing the number of straightforward transfusion events

- concluded group - negative antibody screen

Increasing Electronic Issue proportion

- less cost
- less delay

Reducing antibody investigations

- less cost
- less delay
- less chance of error

Beyond the mandatory – pan reactive antibodies

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Avoiding masked antibodies

Antibody screen		
S1	S2	S3
0	0	0

Antibody screen		
S1	S2	S3
4	4	4

31% - underlying antibodies
11% - non Rh and K (Maley 2005)
Preventing patients forming new alloantibodies

Identification Panel										
P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	Auto
4	4	4	4	4	4	4	4	4	4	4

Alloimmune to high frequency antigen
- Anti-Vel, - Fy3, -U…
- Additional antibodies
- Hard to find compatible blood
- Hard to exclude additional Ab

Identification Panel										
P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	Auto
4	4	4	4	4	4	4	4	4	4	0

So should we match everyone for everything?

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M N

S s

K

Jka Jkb

Fya Fyb

Logistically very difficult

- >400 combinations assuming ABO+D match
- >300 stock holding sites
- phenotyping units is expensive
- phenotypically diverse population

- Matching causes delays
- Most patients will not become alloimmunised
  - (1-4% most commonly to E, K. Gehrie 2014)
- Transfusing high specification units where they are not required, makes them unavailable when they are required!

Easy to match?

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CCDee, K-, M-, S-, Jk(a-b+), Fy(a-b+)

CCDee

K-

M- S-

Jk(a-)

Fy(a-)

1 in 500!

20%

18%

2.7%

0.62%

0.2%

Easy to match?

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ccDEE, K-, s-, Jk(a+b-), Fy(a+b-)

ccDEE

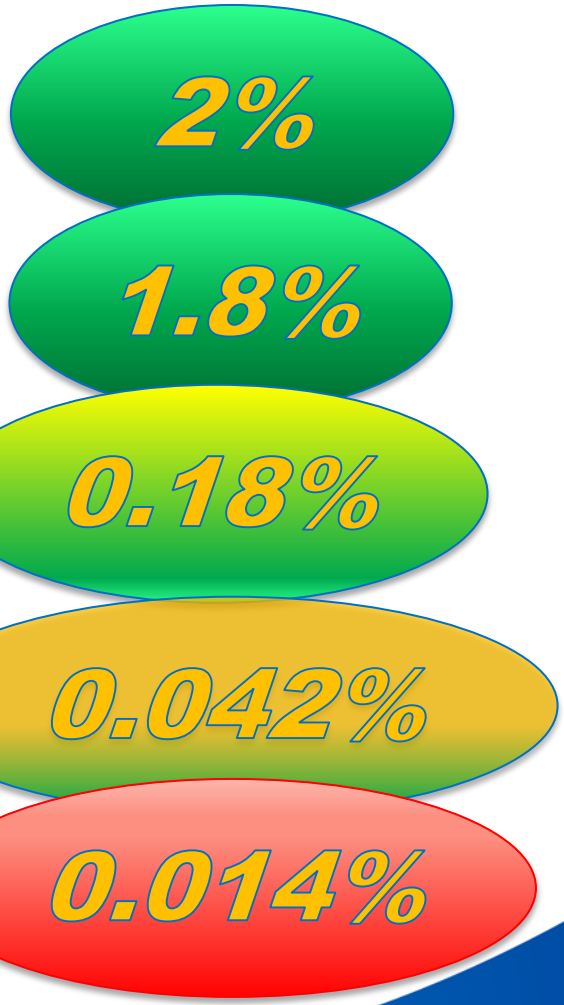
K-

s-

Jk(b-)

Fy(b-)

1 in 7,143!



High risk groups – Sickle Cell Disease

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- Match for CcDEe, K - BSH guidelines (part 1 2016)
- High responder rate (up to 47% C, E, K. Gehrie 2014)
- Establish full phenotype (genotype)
- R_or Supply and demand
- Better to match within ethnic group

7.18.1. There is a high incidence of red cell alloantibodies in patients with sickle cell disease, and severe haemolytic transfusion reactions are not uncommon.
7.18.2. The patient's red cells should be phenotyped as fully as possible prior to transfusion. Where patients have already been transfused, the genotype can be determined
i. An extended phenotype (or genotype) should include C, c, E, e, K, k, Jka, Jk b, Fy a, Fy b, S, s.
ii. If S- s-, then U typing should be performed.
7.18.3. As a minimum, red cells should be matched for Rh and K antigens.
7.18.4. Ro blood should be selected for patients who are Ro if available, otherwise rr.

High risk groups

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MDS

•Very high alloimmunisation rate (58.6%)

•No specific guidance

Thalasaemias

•High allommunisation rate (37%)

•No specific guidance

Therapeutic MoAbs

•Increasing in use

•Anti-CD38, -47

•Fully type patient

•Match CcDEe, Kk

High risk groups - obstetric

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- Mandatory ABO D
- K- for women of childbearing potential
  - High proportion of anti-K transfusion stimulated
- No guidance on CcEe, other than those alloimmunised to Rh
  - Low proportion of anti-c transfusion stimulated
- Immunisation rates 7% anti-D only (before RAADP 1960s)
- Now more typically 1-3% all specificities

Patient testing

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- ABO D mandatory
- Mid risk patients CcDEe, K
- High risk patients: MNSs, (k if K+), Fya, Fyb, Jka, Jkb
- Prospective Phenotype by choice
- If unavailable (IgG sensitisation, previous transfusion) then consider genotype
- SCD Rare alleles at D and CE locus (genotype), Fy(a-b-), U-

Donor Testing

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- ABO, Rh CcDEe, K on all donations
- MNSs, Jka, Jkb, Fya, Fyb on selected donors
  - Target BAME donors
  - Target new donors
- Currently automated conventional serology
- Role of genotyping
  - Cost
  - Reliability
  - Pheno vs Geno
  - ABO

Risk factors for alloimmunisation

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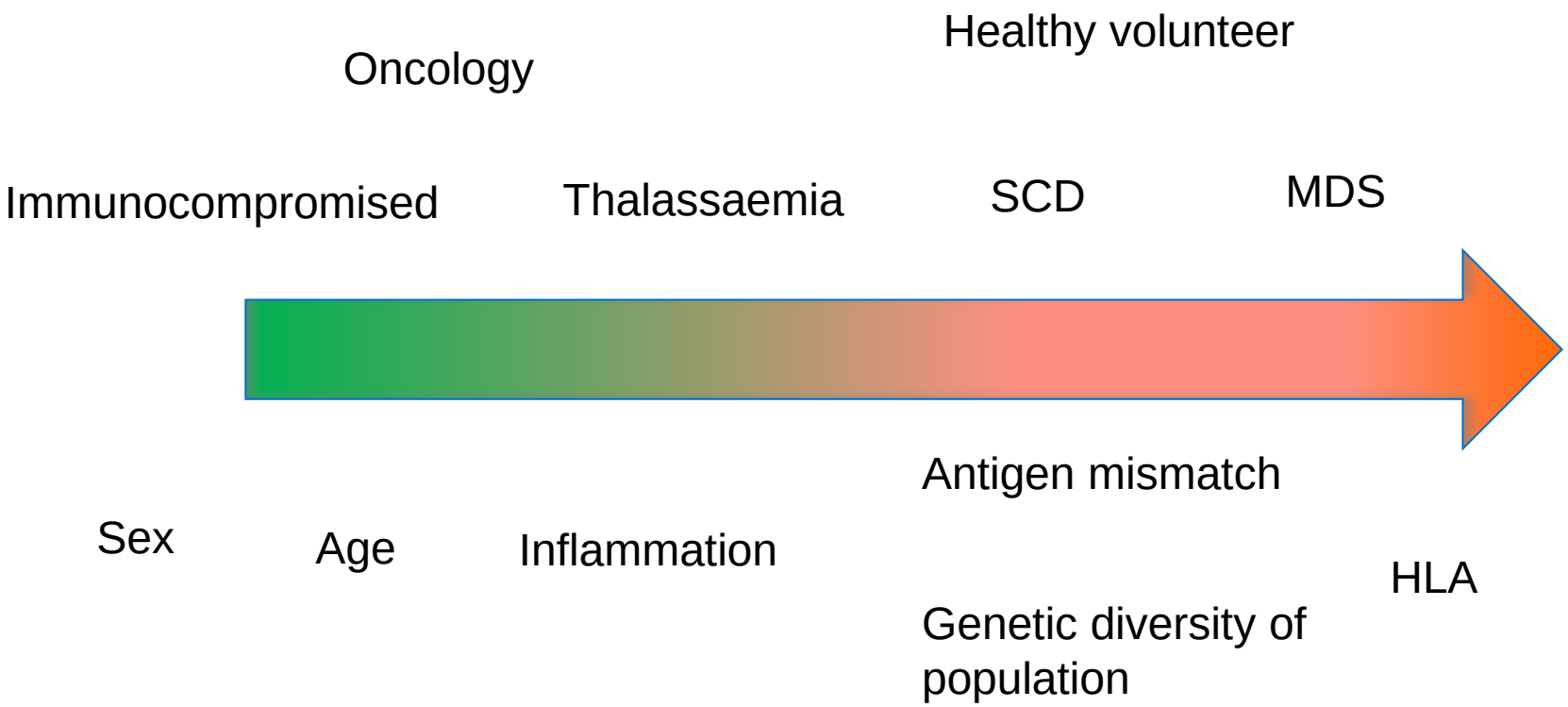

After Gehrie 2014

The responder – the holy grail!

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- Antibody formation has been associated with specific HLA II polymorphisms
  - Mia, Fya, Jka, K, E, S
  - HLA DRB1*15 associated with formation of multiple specificities
  - NHSBT AIR study

The future

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- Population level genotyping
- Epitope matching
- Molecular markers for alloimmunisation
- Might guidelines be more prescriptive?
- Genotype to replace serological testing? (Anani, Transfusion 2017)
  - extensive matching required
  - alloimmunisation remains undetected
  - contrary to BSH guidelines

Summary

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- Matching closely prevents alloimmunisation
- In the UK we have a very diverse population
- There remains a mismatch between distribution of groups of patients and donors
- Matching increases delays, costs
- In most cases, the benefits are small
- In high risk cases the benefits are worthwhile
- Be guided by guidelines
- Consider all risks and benefits, discuss with your supplier before matching more extensively
- Knowing the full type of a patient doesn’t mean we have to match it!
- Patients may become more informed

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Are you my type?

Brunette, 30s, GSoH, likes cinema and negative antibody screens, would like to be matched with tall ccddee, K-, M-, S-, K-, Fy(a-), Jk(b-),

Please send photograph of blood group report.