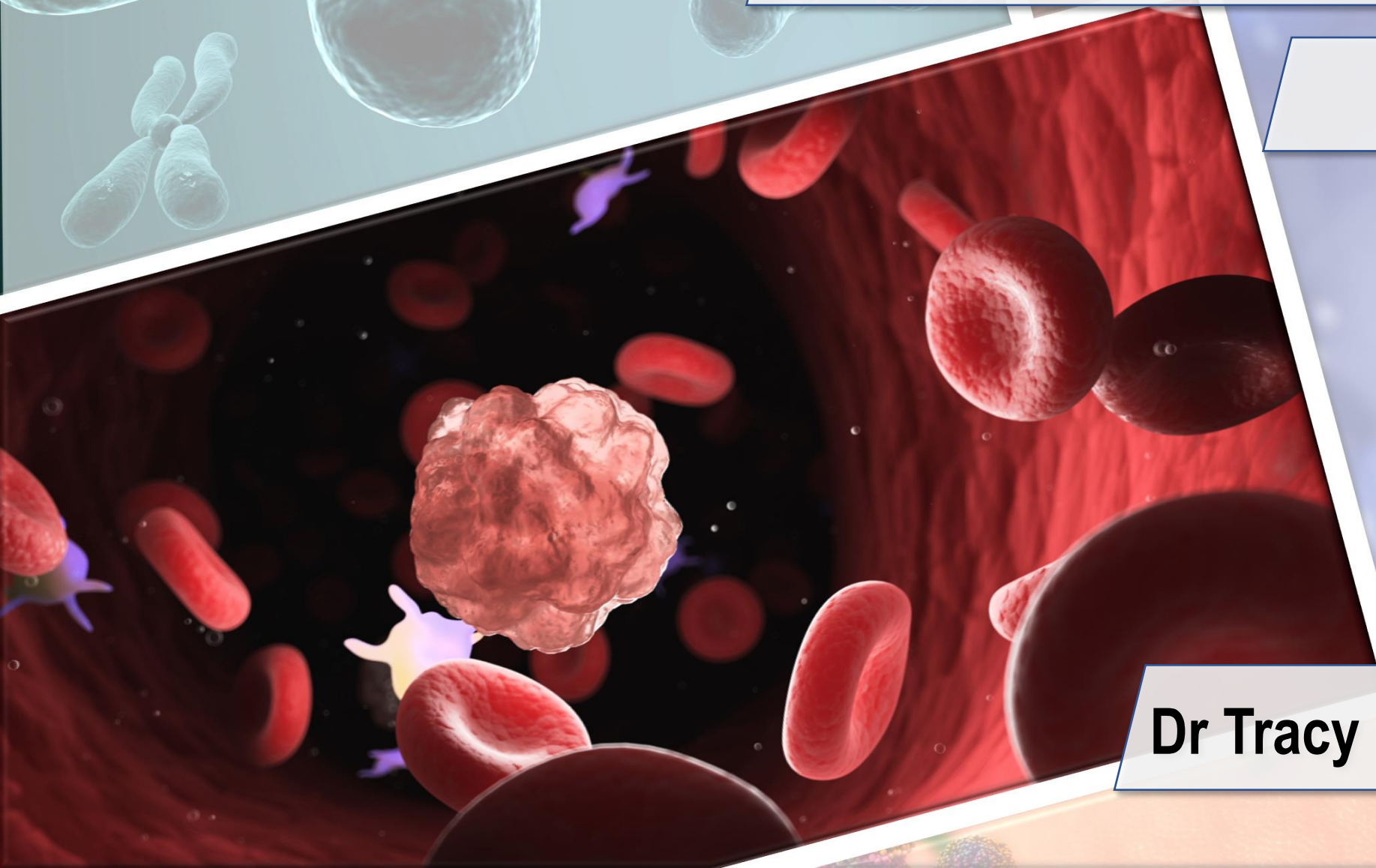
Imperial College London

TBL 4: Transfusion

PART 2



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Session plan

Part 1 – Blood groups and their clinical significance

- Blood group systems
- RBC antigens and antibodies against RBC antigens
- Haemolytic transfusion reaction
- Haemolytic disease of the fetus and newborn
- Naturally occurring antibodies
- Acquired alloantibodies

Part 2 – ABO and Rh blood group systems

- ABO – Antigens, Antibodies, Selecting blood components for transfusion
- RH – Antigens, Antibodies, Selecting blood components for transfusion
- Other blood group systems

Part 3 – Pre-transfusion compatibility testing

- ABO grouping
- RhD grouping
- Antibody screen
- Crossmatch

Part 4 – Donor selection and testing

- Blood donors
- Tests undertaken on donations

Part 5 – Blood components and why we use them

- Whole blood donation
- Apheresis
- Red cells
- Platelets
- FFP
- Cryoprecipitate
- Plasma derived medicinal products

1- POM 2-5 Explain the clinical importance of major blood groups and the screening of blood donors and recall the blood components used in transfusion

ABO BLOOD GROUP SYSTEM

ABO antigens

There are 4 main blood groups within the ABO blood group system: **A**, **B**, **AB** and **O**

- Group **A** individuals express A antigen on their RBCs
- Group **B** individuals express B antigen on their RBCs
- Group **AB** individuals express both A and B antigens on their RBCs
- Group **O** individuals express neither A nor B antigens on their RBCs

ABO antigens

The ABO blood group is determined by a single gene which has **3 alleles: A, B and O**

The A and B antigens are formed by adding specific monosaccharides onto a common glycoprotein and fucose stem (‘H antigen’) on the RBC membrane and this is determined by the corresponding alleles

- The A allele codes for an enzyme that adds N-acetyl galactosamine (GalNac) to the common H antigen resulting in the A antigen
- The B allele codes for an enzyme that adds galactose (Gal) to the common H antigen resulting in the B antigen
- The A and B alleles are co-dominant so presence of both alleles results in formation of both A and B antigens
- The O allele produces an inactive enzyme so the H antigen remains unchanged and neither A nor B antigen can be formed . The O gene is recessive.

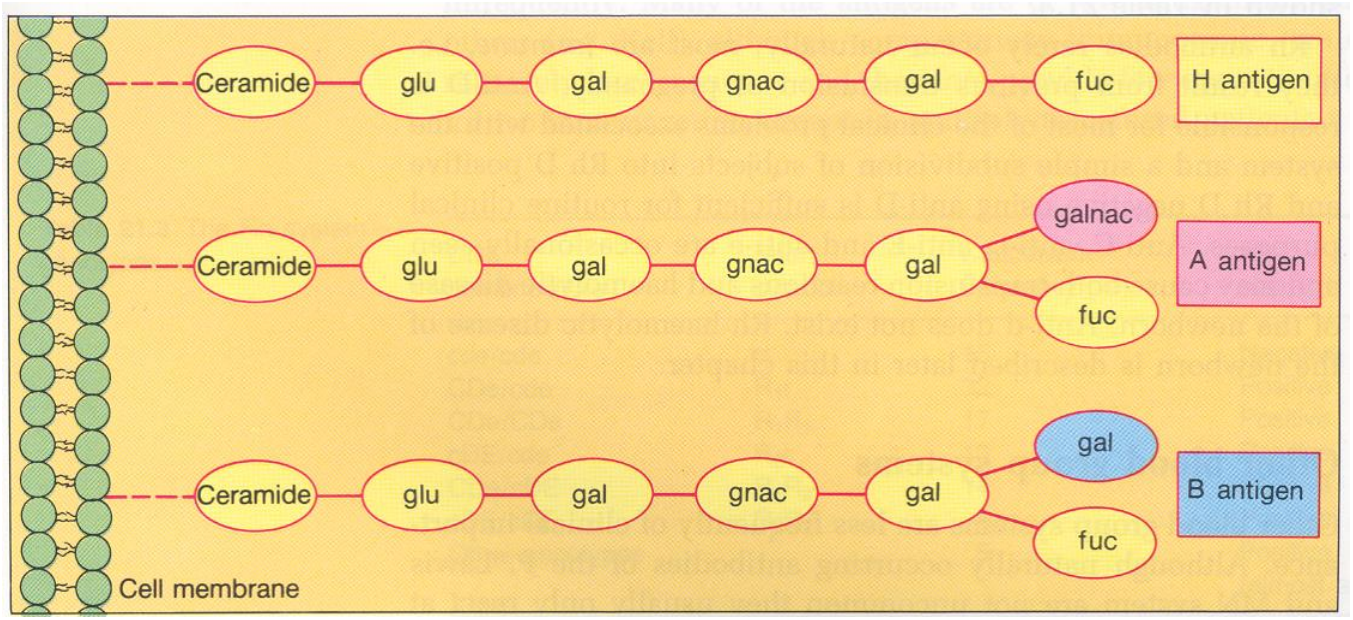

Figure: Structures of H, A and B antigens expressed by blood group O, A and B individuals respectively. Blood group O individuals express the common 'H' antigen.

ABO antigens

An ABO allele is inherited from each parent resulting in the genotype and therefore ABO blood group of the offspring.

ALLELE FROM ONE PARENT	ALLELE FROM OTHER PARENT	GENOTYPE OF OFFSPRING	BLOOD GROUP OF OFFSPRING
A	A	AA	A
A	B	AB	AB
A	O	AO	A
B	A	AB	AB
B	B	BB	B
B	O	BO	B
O	O	OO	O

Figure: Inheritance of ABO blood group system

ABO antibodies

- Within the first few months of life, individuals develop ‘naturally occurring’ IgM ABO antibodies due to the aforementioned antigenic stimuli (*see PART 1*)

- Individuals will develop antibodies against the ABO antigen(s) that they lack

- **Landsteiner's law:**
  - Whichever ABO antigens are lacking on a given person's RBCs, that person will always have the corresponding antibody

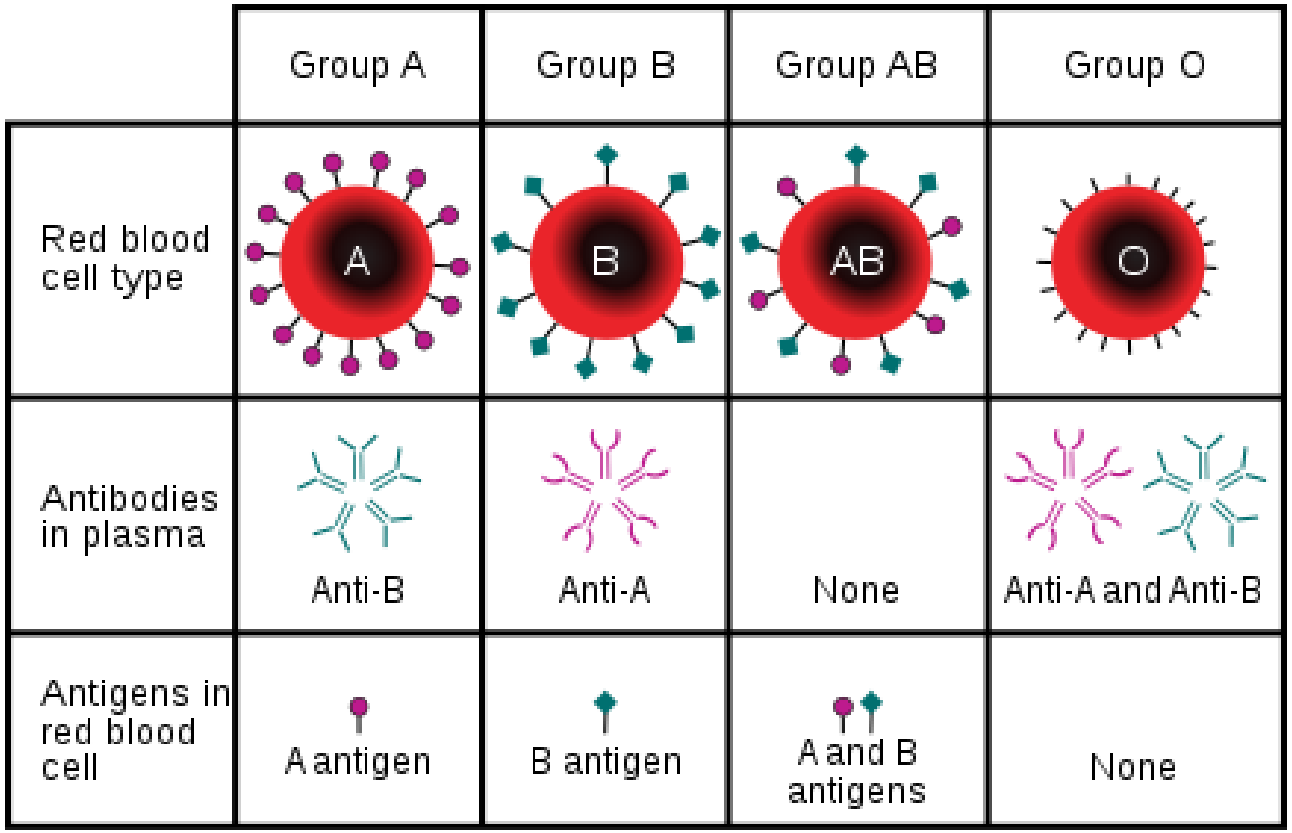

Figure: ABO blood group system showing RBC antigen and corresponding antibodies for each ABO blood group

ABO antibodies

ABO antibodies are mostly IgM antibodies that remain as IgM antibodies throughout life and do not class switch

However, there can also be a **small amount of IgG ABO antibodies** present in the plasma

IgM ABO antibodies

- Can cause **acute HTRs** through activation of the **complement** system resulting in **massive intravascular haemolysis**
- **Cannot** cross the placenta to cause HDFN

IgG ABO antibodies

- **Can** cross the placenta but **do not usually cause HDFN:**
  - Fetal RBCs have poorly developed ABO antigens which are unable to support binding of the IgG antibodies
  - ABO antigens are found on numerous other cells (not just RBCs) so any IgG ABO antibodies that have crossed the placenta can bind to and be 'mopped-up' by these cells
  - The rare cases of ABO HDFN usually occur in mothers who have especially high levels **('high-titre')** of IgG anti-A or anti-B antibodies
  - Any maternal IgG anti-A or anti-B antibodies present at birth in a baby's plasma will disappear within a few months as the baby starts to develop their own IgM anti-A and anti-B antibodies

Selecting blood components for transfusion

- **Red cells**
- **Platelets**
- **Fresh frozen plasma (FFP) or cryoprecipitate**

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- To prevent acute HTRs, **ABO matched** red cells should be selected for transfusion
  - e.g. Group A red cells for a Group A patient

- In emergency situations, where the ABO group of the patient is unknown, **Group O red cells can be given to any patient** (‘**universal donor**’)
  - Group O red cells lack both A or B antigens so there is no risk of acute HTR occurring even if the patient transfused has anti-A and/or anti-B antibodies

Selecting blood components for transfusion

- Red cells
- **Platelets**
- Fresh frozen plasma (FFP) or cryoprecipitate

- Platelets of the **same ABO group as the patient should be selected** for transfusion **where possible** to:
  - **Reduce the risk of a poor response to the platelet transfusion** due to anti-A or anti-B antibodies in the patient's plasma causing destruction of the transfused platelets
    - In reality, this risk is low as the expression of ABO antigens on platelets is low
  - **Reduce risk of haemolysis of the patient's red cells** by anti-A or anti-B antibodies in the transfused unit of platelets
    - Platelets units are made up of platelets suspended in plasma which can contain donor anti-A or anti-B antibodies
    - In reality, risk of haemolysis only occurs in platelet units with high levels **('high-titre')** of anti-A or anti-B antibodies. Platelet units are tested and labelled '**high-titre negative**' if they do not have high levels of anti-A or anti-B in the plasma
- If platelets of the same ABO group as the patient are not available, **platelets of other ABO groups can be transfused as long as they are 'high-titre negative'**
  - e.g. group B individuals can be transfused group A high-titre negative platelets

Selecting blood components for transfusion

- Red cells
- Platelets
- **Fresh frozen plasma (FFP) or cryoprecipitate**

- FFP or cryoprecipitate of the **same ABO group as the patient should be selected** for transfusion **where possible** to:
  - Reduce the risk of haemolysis of the patient's red cells by anti-A or anti-B antibodies in the donor plasma
    - This is only a risk if the plasma contains high levels of anti-A or anti-B antibodies
- If FFP or cryoprecipitate of the same ABO group as the patient is not available, **FFP and cryoprecipitate of other ABO groups can be transfused** as long as they are '**high-titre negative**'
  - e.g. group B individuals can be transfused group A high-titre negative FFP or cryoprecipitate
- Group AB plasma contains no antibodies and can thus be considered the '**universal plasma donor**'

RH BLOOD GROUP SYSTEM

RH antigens

- The Rh system consists of at least 45 antigens

- The most important antigen is **D**
  - **RhD positive** individuals have the D antigen present on their RBCs
  - **RhD negative** individual lack the D antigen on their RBCs

- Other Rh group antigens are: C, c, E, e

- When determining an individual's blood group, as a minimum, we will determine their **ABO group** and their **RhD type**
  - e.g. a patient who is grouped as A positive is group A RhD positive

RH antigens

- The D antigen is inherited as one gene (*RHD*) and the alleles are either ‘D’ or ‘d’
- The ‘D’ allele is dominant and codes for D antigen on the RBC
- The ‘d’ allele is recessive and codes for no D antigen
- If both of a child’s parents are RhD negative (dd), the child will also be RhD negative (dd)
- Otherwise, the child may be RhD positive or RhD negative depending on the specific genotypes of the parents and the alleles inherited

ALLELE FROM MOTHER	ALLELE FROM FATHER	GENOTYPE OF OFFSPRING	BLOOD GROUP OF OFFSPRING
D	D	DD	RhD positive
D	d	Dd	RhD positive
d	D	Dd	RhD positive
d	d	dd	RhD negative

Figure: Inheritance of D antigen

RH antibodies

- Acquired IgG alloantibodies can form as a result of active immunisation (**alloimmunisation**) to 'non-self' RBC antigens following exposure to RBCs from another individual (*see PART 1*)
- Individuals who are RhD negative can make IgG anti-D antibodies following exposure to RhD positive RBCs either through transfusion or pregnancy
- Anti-D antibodies usually become apparent weeks after the exposure
- Once anti-D antibodies are formed, they persist for life

Blood group	Antigen	Antibody
RhD positive	D	None
RhD negative	No antigen	Can develop anti-D antibody if exposed to D positive red cells

Figure: Risk of Anti-D antibody development in D negative individuals

RH antibodies

Anti-D antibodies are clinically significant as they can cause:

Delayed HTR

- Occur when RhD negative individuals who have been alloimmunised and formed anti-D antibodies, are transfused RhD positive RBCs
- We can prevent delayed HTRs by ensuring individuals who have formed anti-D antibodies, are transfused RhD negative RBCs
- It is important to **prevent** the formation of anti-D antibodies in the first place by ensuring RhD negative individuals are transfused RhD negative blood

HDFN

- Can occur when a pregnant RhD negative mother who has been alloimmunised and formed anti-D antibodies, is carrying a RhD positive fetus
  - IgG anti-D antibodies can cross the placenta and haemolyse RhD positive fetal RBCs
  - Severe HDFN can result in intra-uterine death.
  - In less severe cases, the baby survives to birth but there is a risk of severe brain damage from the high bilirubin levels which requires specialist treatment
- We can prevent pregnant RhD negative women from forming anti-D antibodies if they are carrying a RhD positive fetus, by giving **anti-D immunoglobulin injections** during pregnancy
  - Destroys any RhD positive fetal RBCs in the maternal circulation as a result of fetomaternal haemorrhage, before she can make her own anti-D antibodies
- If a RhD negative woman has already developed anti-D antibodies and is carrying a RhD positive fetus, she will require additional monitoring throughout pregnancy

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- Red cells of **same RhD type as the patient** should be selected for transfusion
  - RhD negative red cells for RhD negative patients
    - To prevent the formation of anti-D antibodies
    - To prevent delayed HTRs in those who have already been alloimmunised
  - RhD positive patients can be transfused RhD positive or RhD negative red cells (there is no harm - just wasteful!)

- In emergency situations, where the RhD type of the patient is unknown, **RhD negative red cells should be given**
  - Group O RhD negative red cells ('universal donor') are a precious resource as only 6-7% of blood donors are O RhD negative

Selecting blood components for transfusion

- Red cells
- **Platelets**
- Fresh frozen plasma (FFP) or cryoprecipitate

- Platelets of the **same RhD type as the patient** should be selected for transfusion
  - RhD negative platelets for RhD negative patients

- Platelets do not express D antigen but units of platelets can contain small numbers of donor RBCs or fragments of RBCs that can cause alloimmunisation in RhD negative patients

- If RhD positive platelets *have to* be given to a RhD negative patient (e.g. if no D negative platelets available), risk of alloimmunisation can be reduced by giving anti-D immunoglobulin injection

Selecting blood components for transfusion

- Red cells
- Platelets
- **Fresh frozen plasma (FFP) or cryoprecipitate**

- FFP or cryoprecipitate of any RhD type can transfused regardless of the patients RhD type
- These plasma components do not contain any RBCs

OTHER BLOOD GROUP SYSTEMS

Other blood group systems

- E.g. Kell, Duffy, and Kidd blood groups systems - each have their different antigens
- When providing red cells for transfusion, it is not possible to routinely match for all an individual's RBC antigens.
- Approximately 8% of patients will form an antibody when exposed to 'non-self' antigens
- We try to provide blood which is more extensively matched for individuals most at risk of alloimmunisation such as those who require regular transfusions (e.g. patients with sickle cell disease)
- **Once an individual has developed a clinically significant alloantibody against a RBC antigen, they must be transfused antigen negative red cells to prevent the risk of delayed HTRs**
    - E.g. O RhD negative patient with anti-E antibody – needs O RhD neg and E negative red cells
- Pregnant women who have developed alloantibodies to RBC antigens other than D antigen may also require additional monitoring during pregnancy if the antibody is capable of causing HDFN