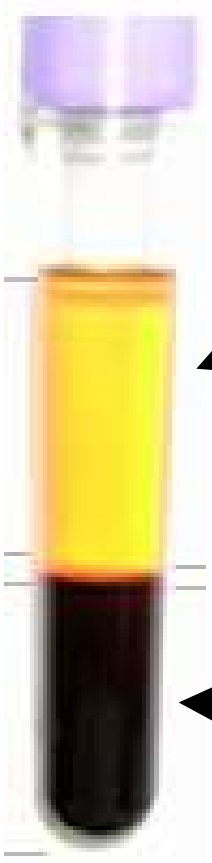
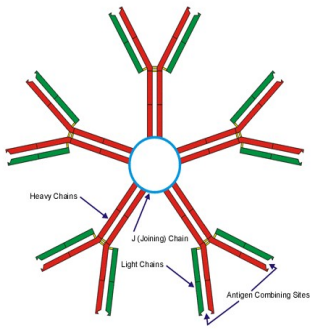
Essentials of Blood Group Antigens and Antibodies

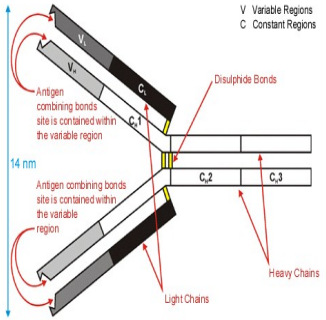
Non-Medical Authorisation of blood Components
Nov 2017

Transfusion Terminology

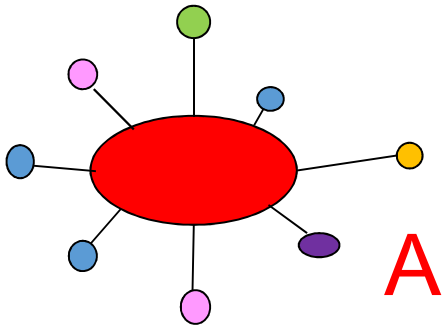
Antigens and Antibodies







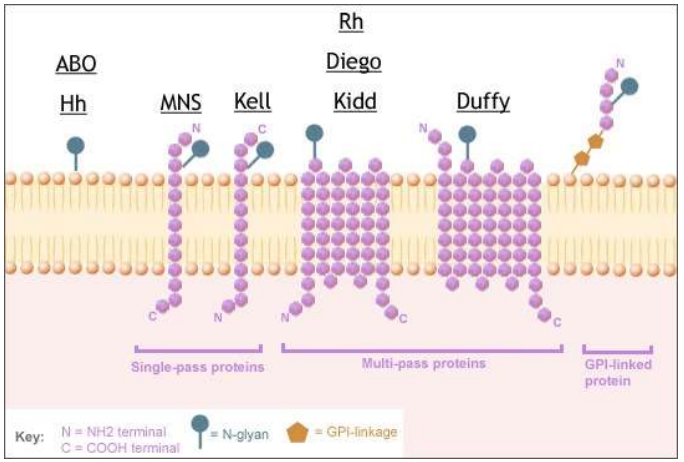
Antibodies



Antigens

Blood Group Antigens

- Antigens are part of the surface of cells
  - Red Cells have "**Blood group antigens**"
  - White cells and platelets have **HLA antigens** (platelets also have **HPA antigens**)

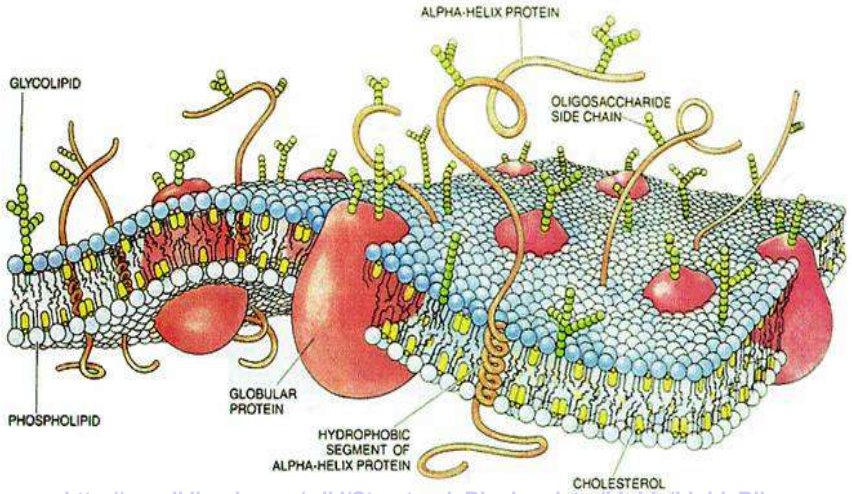


https://www.ncbi.nlm.nih.gov/books/NBK2264/bin/imagemap.jpg

Reactions to blood usually occurs when the antigen on the donor cells reacts with an antibody in the patient's plasma

What Are Blood Group Antigens?

- Complex structures that contain protein and carbohydrate
- Part of the membrane structure
  - blood group antigens often have a role e.g. structural, transport
- Produced by inheritance of specific genes
  - genes produce different antigen options within one blood group system



http://en.wikibooks.org/wiki/Structural_Biochemistry/Lipids/Lipid_Bilayer

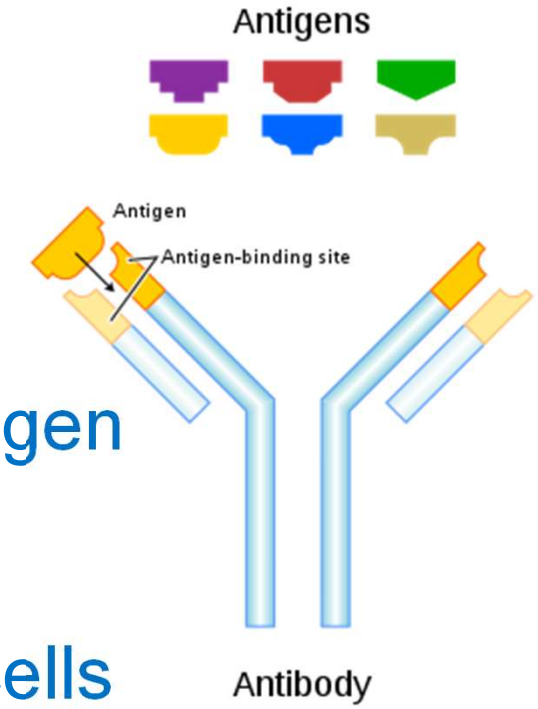
Blood Group Antigens

- Currently 36 known blood group systems
- Most clinically important are ABO and Rh
- Antigens on **donor red cells** can stimulate a patient to produce an **antibody**, if the ***patient lacks*** the antigen themselves
- Likelihood of antibody production is low but increases the more transfusions that are given

What are Blood Group Antibodies?

- Protein molecules - called immunoglobulins (Ig)
- Found in the plasma/serum
  - Produced by the immune system following exposure to a foreign antigen
  - Antibodies bind specifically to the corresponding antigen on the red cells
  - In the body this usually results in the destruction of the red cell

https://en.wikipedia.org/wiki/Antibody#/media/File:Antibody.svg



Antibodies Are Stimulated by

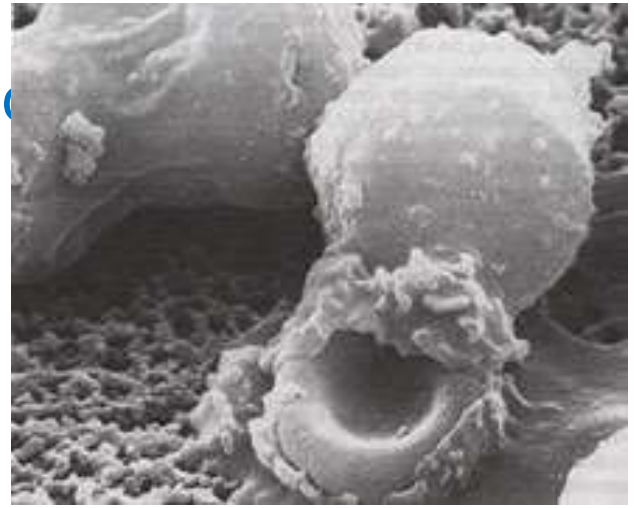
- Blood transfusion

  i.e. blood carrying antigens foreign to the patient
- Fetal antigen entering maternal circulation during pregnancy or at birth stimulating antibody in mother
- Environmental factors (ie naturally acquired as with anti-A and anti-B)

Antibody - Antigen Reactions

IN VIVO (*in the body)*

- Leads to the destruction of the cell either
  - directly when cells break up in the bloo stream INTRAVASCULAR
  - indirectly where the liver and spleen remove antibody coated cells EXTRAVASCULAR



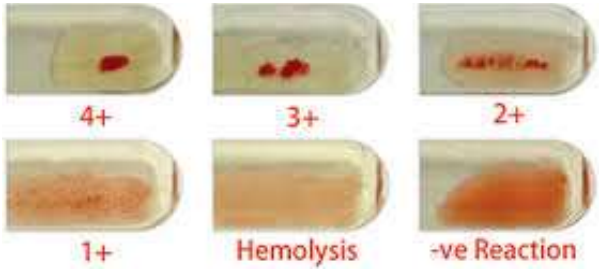
http://www.epidemic.org/thefacts/viruses/theHostDefenses/

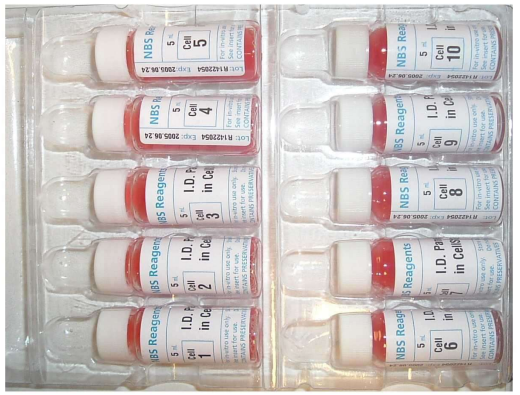
IN VITRO *(in the lab)*

- reactions normally seen as agglutination
- blood transfusion tests utilise these specific antibody-antigen reaction

Agglutination

- Clumping together of red cells into visible agglutination
- Antibody cross-links with the antigens
- The reaction is specific, so agglutination can be used to identify the presence of
  - Red cell antigens i.e. ‘blood grouping’
  - Antibody/ies in the plasma i.e. ‘antibody screening’, antibody identification
  - An incompatible crossmatch





ABO & Rh Blood Group Systems

The ABO Blood Groups
What do you know?

- Discovered by in 1900
- Simple inheritance of 3 gene options A, B or O giving four possible groups - A, B, AB and O
  - A and B genes are co-dominant

The most clinically important blood group system

- 'Natural' presence of ABO antibodies

Landsteiner's Law

When an individual lacks the A or B antigen the corresponding antibody is produced in their serum/plasma

Inheritance

Group	Antigen Phenotype	Antigen Genotype
O	O	*OO*
A	A	*AA or AO*
B	B	*BB or BO*
AB	AB	*AB*

ABO Antigens & Antibodies

Complete the table

Red Cell Type		Antibody present
Blood group	Antigen present	
O	No A or B Antigen	Anti-A, Anti-B (Anti-A,B)
A	A Antigen	nti-B
B	B Antigen	Anti-A
AB	A and B Antigen	No antibodies

ABO Compatibility

35% chance of mismatch!	Recipient Blood Group			
Donor Blood Group	O	A	B	AB
O				
A				
B				
AB				

- Compatible: Patient survives

- Incompatible: Potentially fatal

Intravascular Haemolysis

Frequency in UK

Group	Approx. Uk Frequency %	Antibodies
O	45	Anti-A & B
A	43	Anti-B
B	9	Anti-A
AB	3	None

- Group B is more common in Asian population (35%)
- Some African tribes are 100% group O

The Rh Blood Group System

- Discovered by Levine and Stetson (1939)
  - Antibody found in a woman who had given birth to a stillborn baby and subsequently had a transfusion reaction

  What condition could have caused the death of the baby?

- Main antigen is called D
- Complex system - other important Rh antigens are C, c & E, e

D Antigen- Frequency variations

- People with D antigen are D positive (85% in UK)
- People who lack the D antigen are D negative (15% in UK)
  - 5 - 10% in black and 0.3% in Chinese populations
- When exposed to the D antigen up to 80% of D negative people produce anti-D

The Rh Blood Group System

When might Anti-D be stimulated?

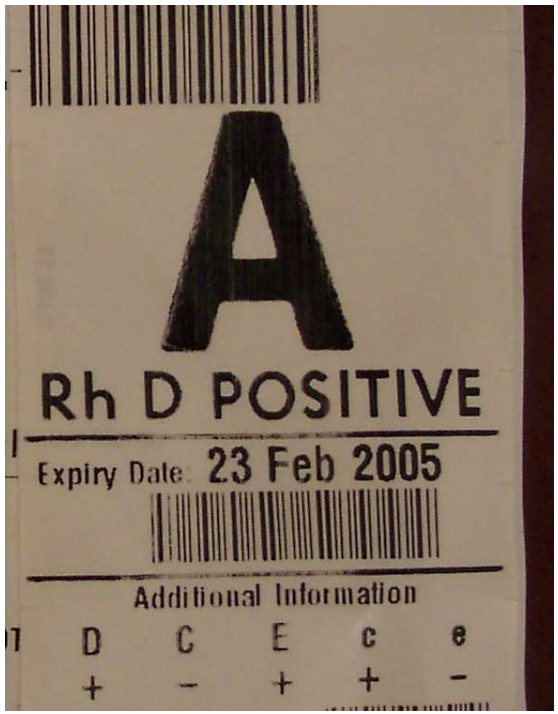
- Most important blood group system with regard to Haemolytic Disease of the Fetus or Newborn (HDFN)
- Second only to ABO with regard to transfusion
  - Other Rh antigens are less immunogenic - C, c, E & e
  - The most commonly produced Rh antibody after anti-D is anti-c usually produced in D positive people

Blood Provision

- D negative females of childbearing potential **must only** be given?
  - D negative red cells or platelets
- Can you ever give D Positive blood to a D negative patient?
- Patients with an Rh antibody must have antigen negative blood:-

Which patient/s could you give this unit to?

- Patient with Anti-D - N
- Patient with Anti-C - Y
- Patient with Anti-E - N
- Patient with Anti-c - N
- Patient with Anti-e - Y



Other Blood Groups

- 36 blood group systems including ABO and Rh
- Nine are considered ‘major’ blood group systems
- How many can you name?

- Each blood group system has (at least) two alternative gene (and therefore antigen) possibilities

How many can you name?

System Name
1. ABO
2. Rh
3. MNS
4. P1PK
5. Lutheran
6. Kell
7. Lewis
8. Duffy
9. Kidd

Less clinically significant than ABO or Rh

But...

Many are capable (if infrequently) of stimulating clinically significant antibodies

2-9% of patients who require a red cell transfusion have red cell antibodies

How can you find out which are clinically significant?

BSH guidelines

Antibodies of the same specificity have different degrees of significance!

- ***Transfusion***
  - Immediate destruction of (some of) the transfused red cells (within hours or even minutes)
  - Reduction of expected red cell survival
  - No discernable red cell destruction

- ***Pregnancy***
  - Fetal death due to HDFN
  - Positive Direct Antiglobulin Test (DAT) and clinical evidence of HDFN
  - Positive DAT without clinical evidence of HDFN

Sometimes we have no idea!

Pre-transfusion Testing

The Aim of Pre-transfusion Testing

- To provide blood that is safe for transfusion
  - No transfusion reaction
  - No reduced red cell survival

- To have advance notice of transfusion requirements
- What do you need to know before selecting blood for a patient?
  - The patient's ABO and D group
  - Are there any unexpected antibodies
  - How easy will it be to provide compatible blood

Role of the Hospital Blood Bank

- To provide the right blood component(s), to the right patient at the right time
  - Pre-transfusion Testing
    - ABO/Rh(D) typing of recipient
    - Antibody screen & identification
  - Select the unit(s) to be transfused
    - Electronic Issue or Serological crossmatching?

Sample Requirements

WBIT - Wrong Blood in Tube

- How should it be prevented?
- How can it be managed?

SPECIMEN COLLECTION
- Verify patient identity
- Match ID band to specimen labels
- Affix labels at the bedside

PRETRANSFUSION
- Two separate blood samples
- Two witnesses at sample collection
- Verify identity, affix labels at bedside

www.slideshare.net/AngeliLagasca/wrong-blood-in-tube-errors-legal-issues-and-recommendations

It has been estimated that

1:2000 samples is from the wrong patient.

Dzik et al 2003 and Murphy et al 2004

New Patients - How many blood samples are required and what is the time scale?

BSH Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories (2012)

Appendix 7: Requirement for two samples for ABO/D grouping prior to the issue of red cells

Concerns have been expressed that the two samples may be taken at the same time, but one 'saved' to send to the transfusion laboratory at a later time. It is important to have a policy and process in place to assure that the two samples have been taken independently of one another, and those taking samples for transfusion, need to understand the reasons for requesting a second sample and the risk of WBIT.

Based on BEST studies and SHOT reports

Blood Grouping

The first step in pre-transfusion in the compatibility testing process is

- ABO and D grouping - routinely performed on every hospital patient requiring / potentially requiring a blood transfusion
  - ABO and D grouping is also routinely performed on every blood donation (NHSBT)
- So that ABO and D matched blood can be selected for transfusion

Antibody Screening and Identification

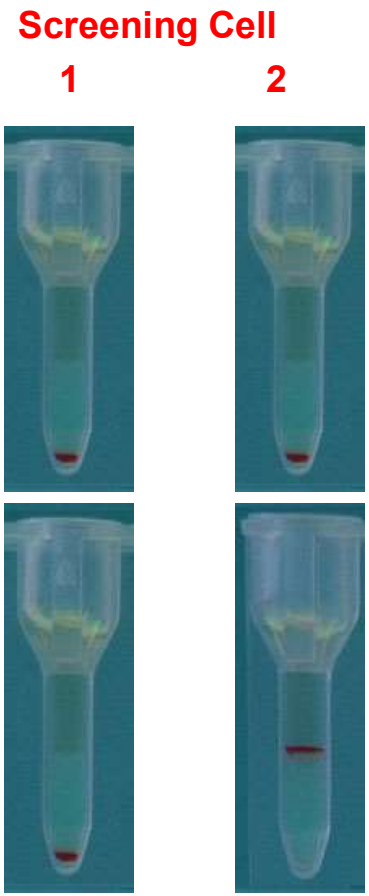
The second step in pre-transfusion compatibility testing

- Testing patients plasma prior to transfusion:
  - looking for unknown red cell antibodies in the patient's plasma using cells with known antigens
  - 2-3 cells (screening) or 8-12 cells (identification)

X

Unknown
plasma

Antibody Screening



Tests for the presence of antibodies to antigens of the other major blood groups

- A negative result (no agglutination) indicates that no significant red cell antibodies are present
- A positive result (agglutination) indicates the presence of an antibody in the recipients plasma

BUT this just tells us antibody is present. It does not tell us what it is or how clinically significant it is!

Antibody Identification

- Once an antibody has been detected we determine the antibody specificity
- The answer will indicate the 'clinical significance'
    - do the antibodies react at 37°C

- *In vivo* can the antibody
    - cause patient morbidity due to accelerated destruction of transfused red cells
    - shorten the survival of transfused red cells
    - cause HDFN

Selection of Red cells for Transfusion

- Most people who need blood have “off the shelf” donations
- Matched for ABO and D
- The selection of suitable red cells will be made either by Electronic Issue or by Serological Crossmatch

Electronic Issue

- Electronic Issue of red cells for transfusion is the selection of donor units from blood bank stock of the same ABO/D type by the blood bank computer
- This form of red cell selection is **only** suitable for patients when
  - Testing and result entry is fully automated
  - There are no blood group discrepancies
  - The antibody screen is negative

- Computer software must be validated to ensure that ABO-incompatible blood cannot be reserved or issued

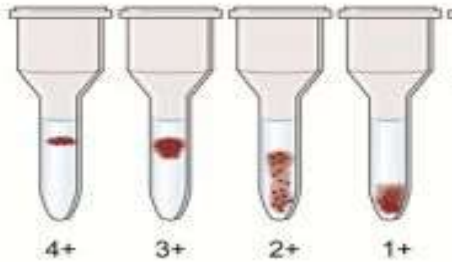
Serological Crossmatch

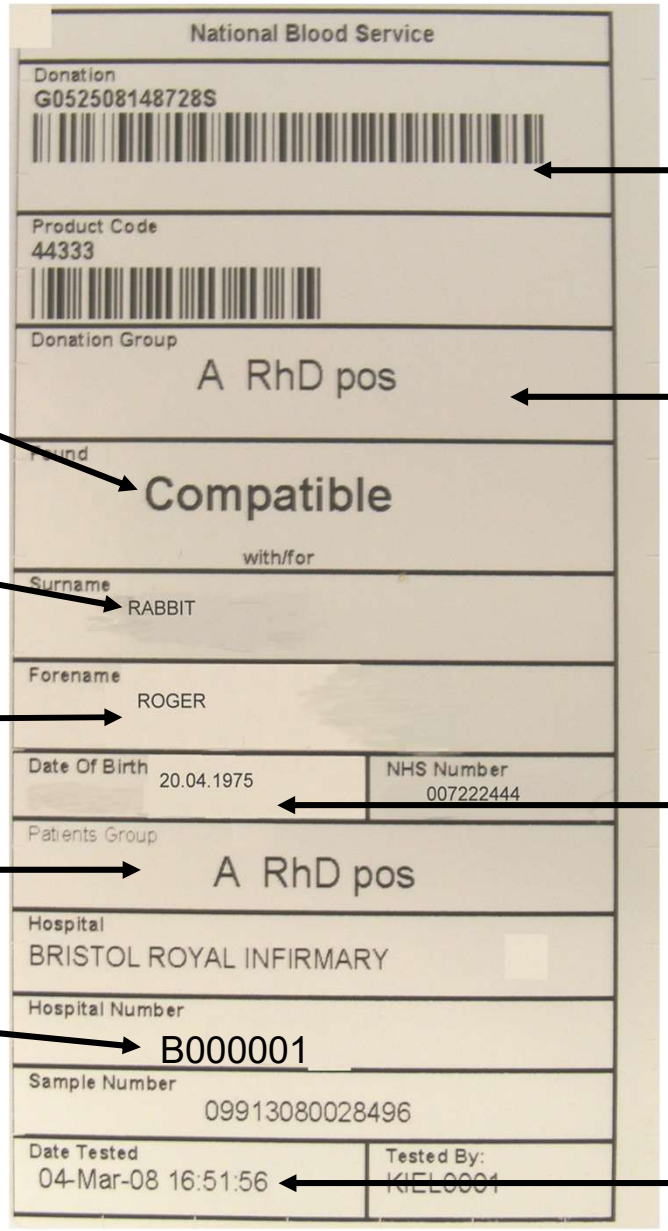
- Suitable for all patients
- Reacting plasma from the patient with the red cells from the proposed donor unit
  - Must be ABO/D compatible and if required antigen negative

Patient's plasma X Donor's red cells

Negative crossmatch

Positive crossmatch





Donation number

Donation blood group

Crossmatch result
Compatible / Suitable

Patient's surname

Patient's first name

Date of birth

Patient's blood group

Hospital number

Date tested

Providing Antigen Negative Units

- ABO group of your patient
- D matched (Rh matched)
- Antigen negative for any clinically significant antibodies detected
- Any specific requirements?

Blood Provision

- Supply of antigen negative blood for transfusion cannot in practice be based on specificity alone
- Other factors that may need to be considered are
  - How urgently blood is required
  - Are they bleeding and how much blood is needed
  - Whether the patient is immunologically compromised and unlikely to respond
  - The risk of transfusing incompatible blood should only be considered when it is outweighed by the risk of not transfusing'

BSH guideline information should be followed

What might happen if we get it wrong?

The selection and issue of red cells are inherently high risk procedures

- If something is missed the patient may have a Transfusion Reaction
- Intravascular removal (haemolysis) in blood vessels
  - Free haemoglobin released
  - Extravascular removal of red cells with antibody principally in the spleen/liver