NORTH EAST & YORKSHIRE REGIONAL TRANSFUSION COMMITTEE

NHS Blood and Transplant

Clinically Significant Antibodies and the Provision of Blood Components

Presented by the North East & Yorkshire Non-Medical Authorisation working group

Caring Expert Quality

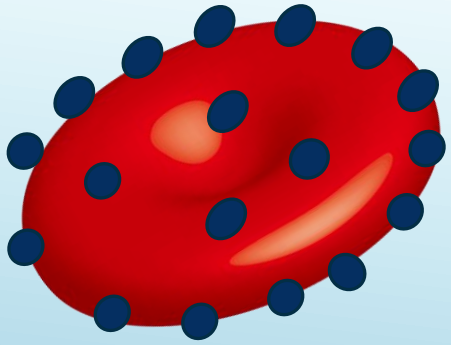
Aims

- What is a Clinically significant Antibody
- Pre Transfusion testing process
- When are antibodies a problem
- How we provide blood for these patients

- What's happening 'behind the scenes' to your sample

What is an antibody… transfusion talking

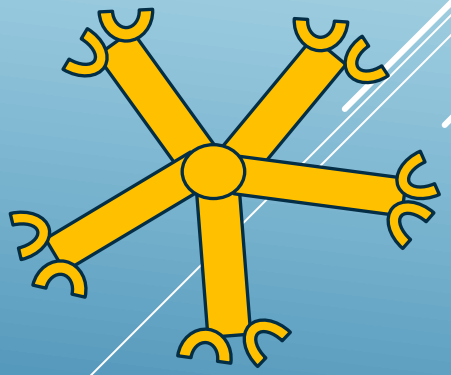
- Antigen – Specific protein(s) found on the cell surface



- Antibodies – if present, circulating in the patient, are immunoglobulins which can bind to a specific antigen on the cell.

IgG – monomers with 2 binding sites; cannot directly agglutinate, but will activate compliment when bound to antigen site, flagging cells for destruction

IgM – pentamers = 10 binding sites; capable of direct agglutination



Where do antibodies come from

- In order for the body to make an antibody… it must first 'see' the antigen* – this is sensitisation
- Sensitisation occurs in 1 of 2 ways…
  - Transfusion
  - pregnancy
- So on a sensitisation event the patient will not react to a component as it is about to produce the antibody…
- The next time a patient sees that Antigen they have the Antibody to.. It will likely react against it .. And potentially cause a reaction..
- That said… Not all transfusion reactions are because of antibodies!

* Exception to the rule being ABO antibodies…

Clinical significance

Only antibodies detected which have the ability to shorten or destroy red cell survival are deemed clinically significant.

This normally means by causing a Haemolytic Transfusion Reaction or Haemolytic Disease of the Foetus and Newborn (HDFN) – Anti- D and Anti- K are two particularly problematic antibodies in HDFN.

They are active at 37°C

- Alloantibody = Directed against a foreign red cell (e.g transfused cells) resulting in transfusion reaction (e.g Anti-D in RhD Neg patient)
- Autoantibody = directed against patients own red cells (e.g Anti-D in RhD Pos patient) = Autoimmune Haemolytic anaemia

There are lots of different red cell antigens on the cell surface,

…..but it's not necessarily the same for antibodies circulating …

ABO/ D group summary

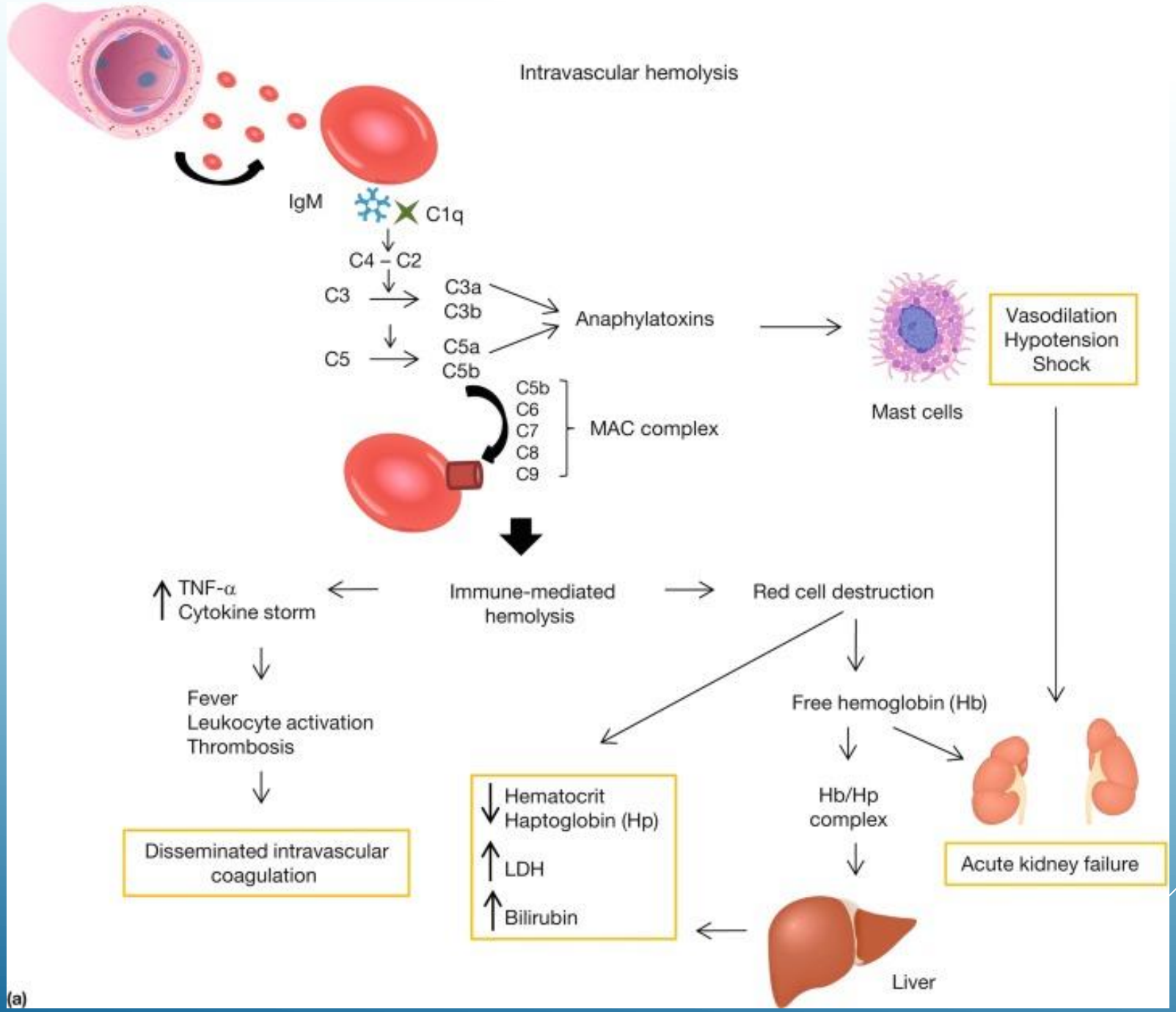
ABO BLOOD GROUPS	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in Plasma	 Anti-B	 Anti-A	NONE	 Anti-A and Anti-B

RhD Pos	RhD Neg
Antigen Present	No antigen
No allo-antibody production..	Possible antibody production if sensitised

ABO

- Naturally occurring innate antibodies
- IgM pentamers, cannot cross the placenta therefore don't affect the foetus during pregnancy, but are capable of activating complement causing **immediate intravascular haemolysis**….
- So ABOi transfusion can cause catastrophic and even fatal consequences to our patients… but is avoidable!

Blood Group	% UK population
O Pos	35 %
A Pos	30 %
O Neg	13 %
A Neg	8 %
B Pos	8 %
B Neg	2 %
AB Pos	2 %
AB Neg	1 %


Intravascular hemolysis
IgM
C1q
C4 – C2
C3
C3a
C3b
C5
C5a
C5b
Anaphylatoxins
C5b
C6
C7
C8
C9
MAC complex
Mast cells
Vasodilation
Hypotension
Shock
TNF-α
Cytokine storm
Immune-mediated hemolysis
Red cell destruction
Fever
Leukocyte activation
Thrombosis
Free hemoglobin (Hb)
Hb/Hp complex
Hematocrit
Haptoglobin (Hp)
LDH
Bilirubin
Disseminated intravascular coagulation
Acute kidney failure
Liver
(a)

Why RhD type then?

- D antigen is very immunogenic – approx. 30% of RhD Neg patients who are sensitised will produce an Anti-D antibody..
- Can cause Transfusion reactions….
- But because it is IgG (), it is a smaller protein, and can cross the placenta – this can very problematic in pregnancy as will cause severe (and sometimes fatal) HDFN

What about emergency groups…..

O NEG is the "universal donor" for emergency settings – PBM though for adult male patients or patients of non-child bearing potential (>50yo female) *emergency O Pos can be used* .. emergency only!!! Check your local policy!!!

Blood Group	% UK population	Compatible groups for transfusion
O Pos	35 %	O Pos, **O Neg**
A Pos	30 %	O Pos, **O Neg**, A Pos, A Neg
O Neg	13 %	**O Neg**
A Neg	8 %	**O Neg**, A Neg
B Pos	8 %	O Pos, **O Neg**, B Pos, B Neg
B Neg	2 %	**O Neg**, B Neg
AB Pos	2 %	O Pos, **O Neg**, A Pos, A Neg B Pos, B Neg
AB Neg	1 %	**O Neg**, B Neg, A Neg

Laboratory Testing

- Check patient details against sample and LIMS and any special requirements if known
- Determine the ABO group and Rh D type for the sample
- Identify any irregular antibodies

- component selection and labelling
- Transfusion reaction testing

Samples and forms

- Right patient → Right blood
- Check the sample details against the form – zero tolerance to errors
- Any errors are rejected – patient safety = WBIT
- Sufficient sample to test
- And correct sample if check group/ 2nd sample.

	REQUEST FORM	SAMPLE
Unique Patient ID Number * Can be Hospital number or NHS number	Essential	Essential
Forename	Essential	Essential
Surname	Essential	Essential
Date of Birth	Essential	Essential
Date	Essential	Essential
Time	Essential	Essential
Signature	Essential	Essential
Requesting clinician Name	Essential	N/R
Requesting clinician Signature	Essential	N/R
Clinical information/ test(s) required	Essential	N/R
Sample source if not peripheral blood	Essential	N/R
Special requirements	Essential	N/R

2 sample rules

- Guidelines for pre-transfusion compatibility procedures on blood transfusion laboratories

Key recommendation 12:

Unless secure electronic patient identification systems are in place, a second sample should be requested for confirmation of the ABO group for a first time patient prior to transfusion, where this does not impede the delivery of urgent red cells or other components.

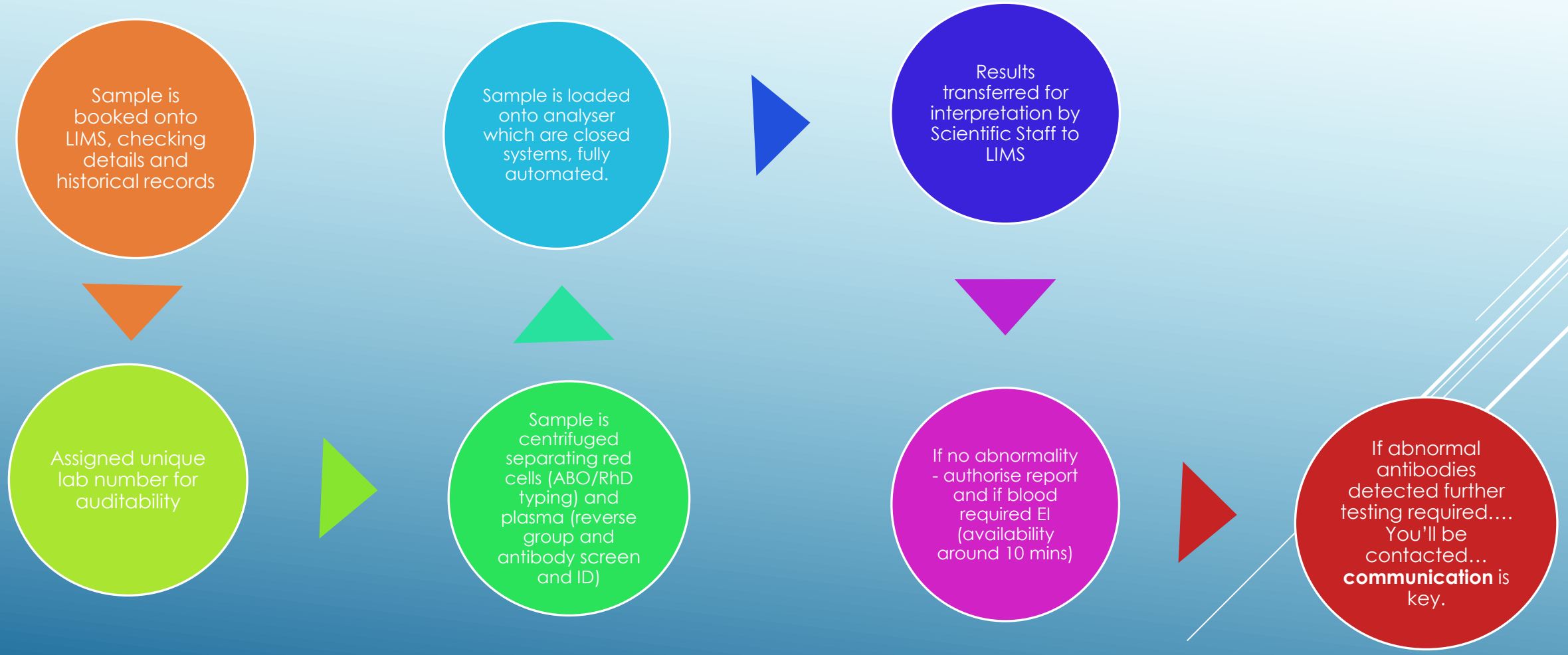
- Most Trusts operate a 2 sample system, check local policy to see how it is implemented but fundamentally it will require 2 independent transfusion samples to be sent to the laboratory.

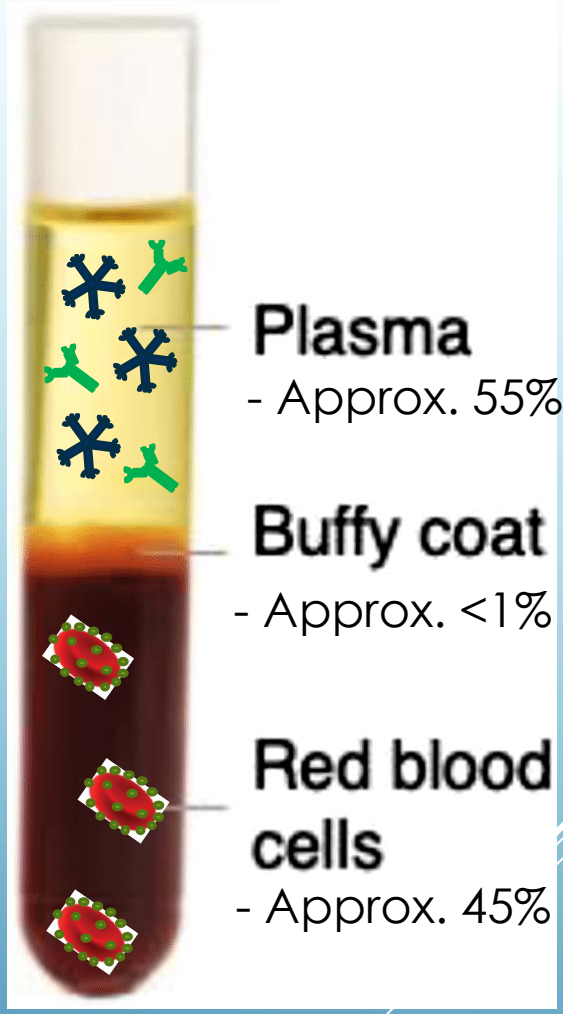
- Why bother? PATIENT SAFETY! It is the only way to detect Wrong Blood in Tube (WBIT) events, which if undetected, may result in ABOi Transfusion = Not good for the patient.

TIME

- On average the time taken to process a Groups and save is approximately 1 hour
- To get EI components 30 minutes
- To get Cross-match components 1 hour
- Plasma and platelet components will be different depending on local policy.
- Urgent/ and emergency settings may be different so it is vital you **speak** to your blood bank team.

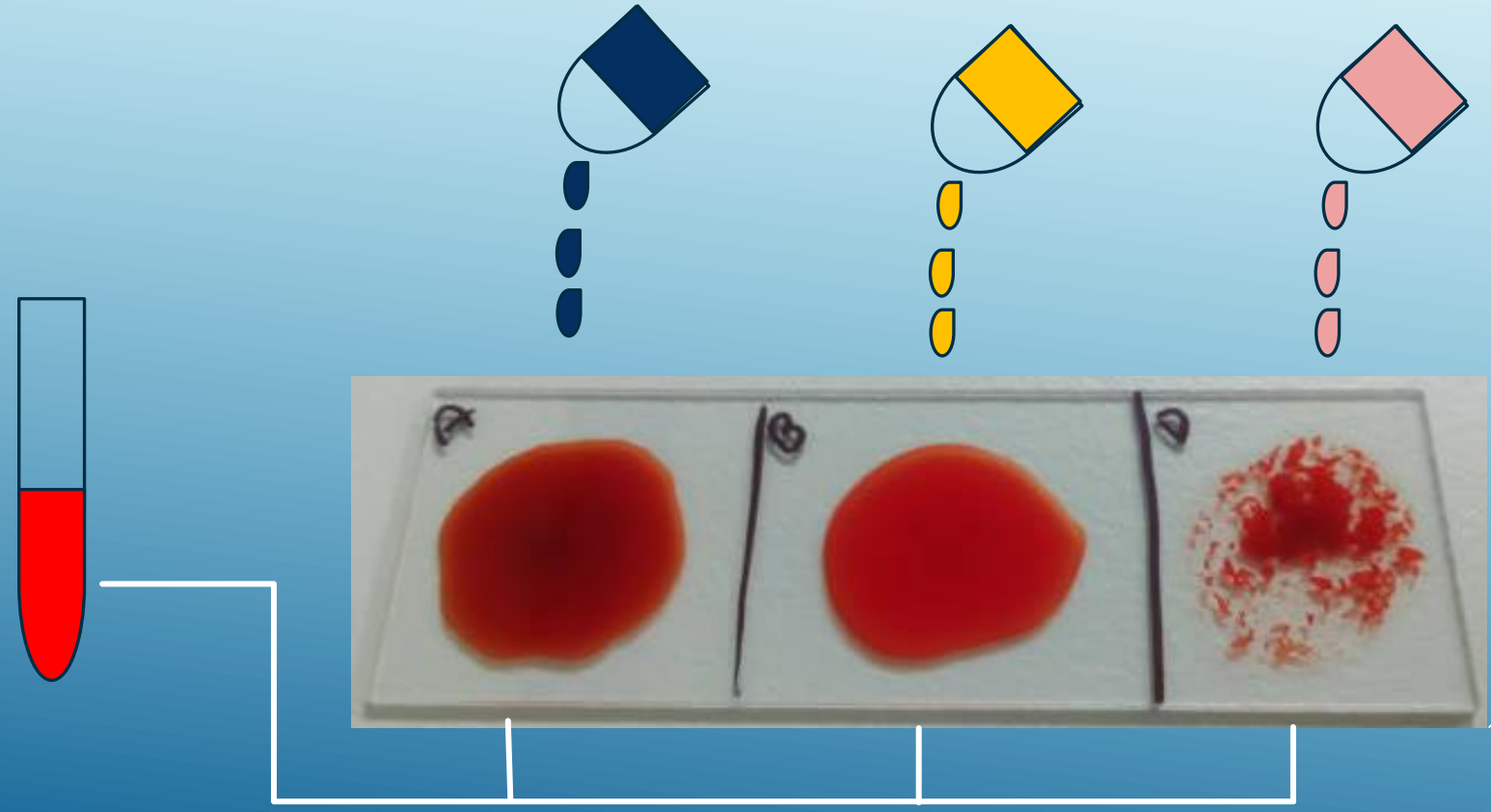
Sample processing



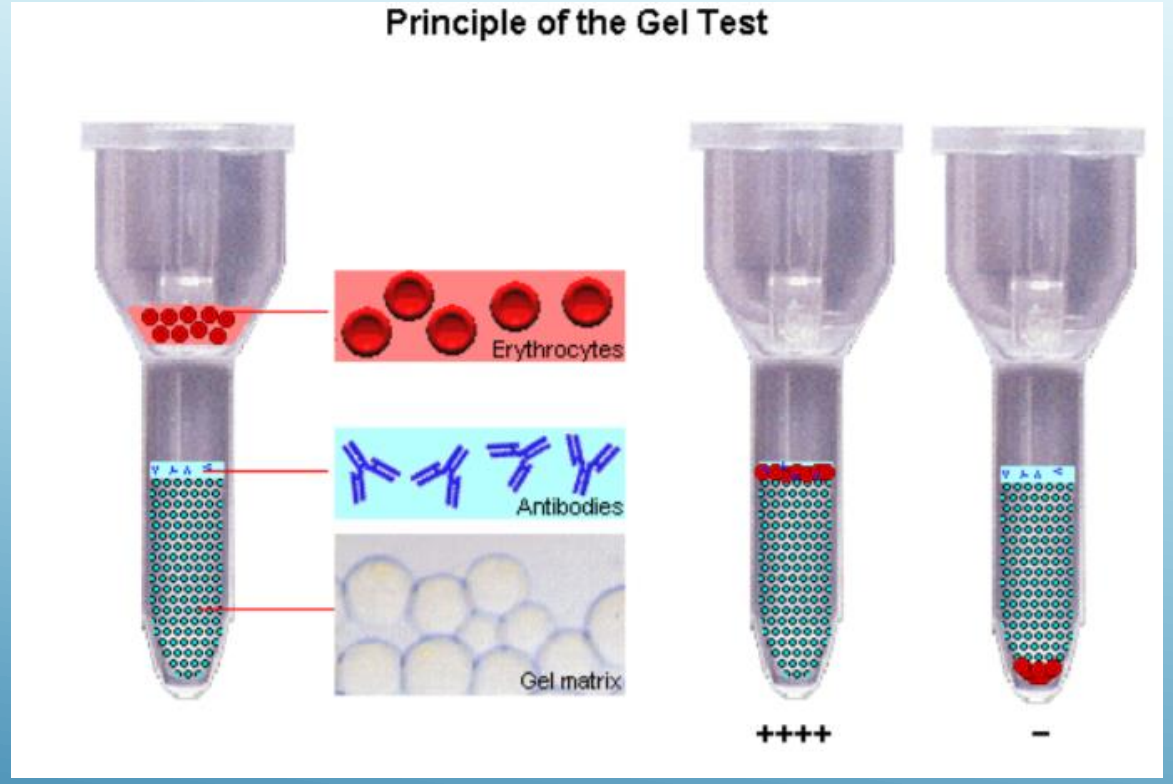

Plasma
- Approx. 55%
Buffy coat
- Approx. <1%
Red blood cells
- Approx. 45%

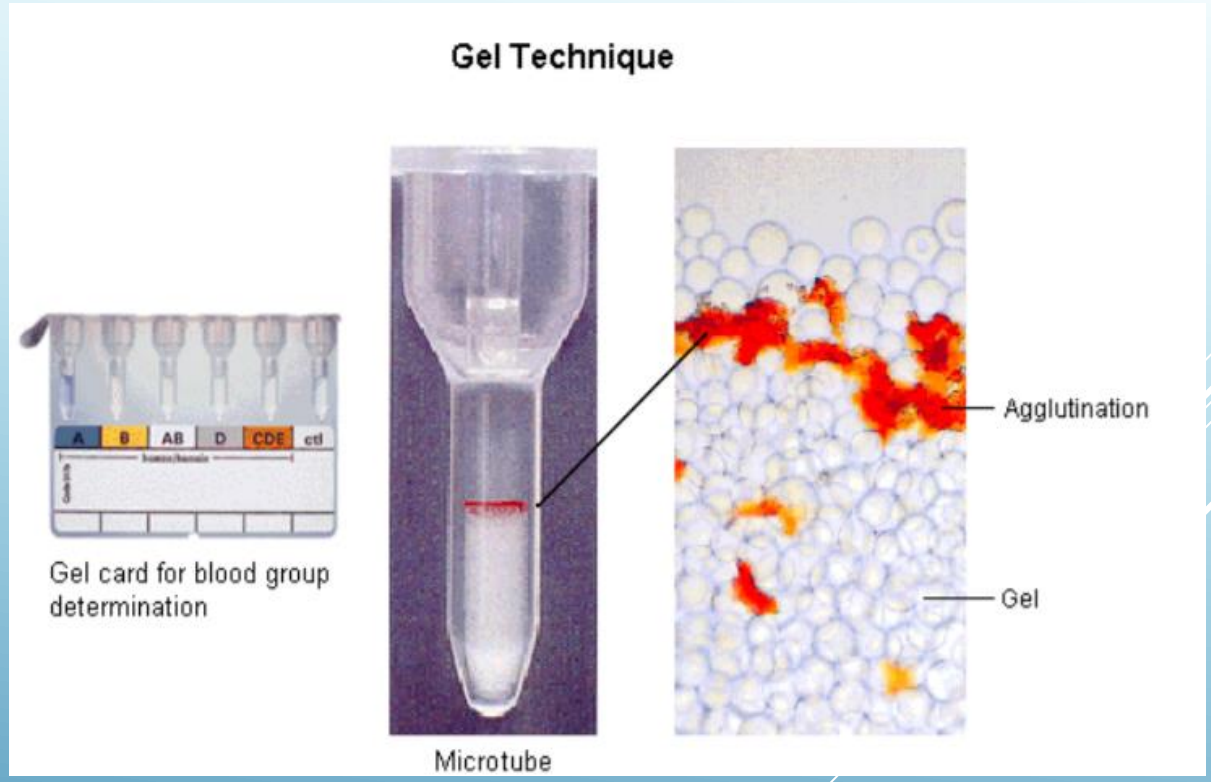
The Testing Technology

- Most systems use gel technology, there are others, **but all use similar basic principles – agglutination!**



Gel Technology





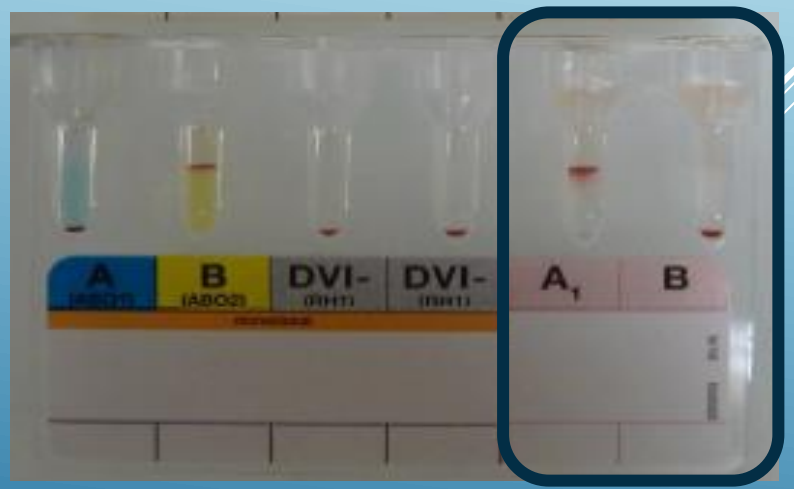
analysers

- Automated – walk away systems to minimise human intervention/ error
- Interfacing between LIMS and analyser to hold results and prompt investigation from laboratory staff.
- Digital record of results for review at a later point e.g. incident investigation or group anomalies.
- Higher through put to enable efficient processing of work and dedication to specialised testing.

ABO/ Rh D typing

- Testing the patients red cells for the presence A and/or B Antigens and presence of RhD Antigen (forward group)

- Test the patient plasma for the antibodies anti-A or Anti-B (reverse group) this allows for the checking of the ABO group. Only for ABO type though.

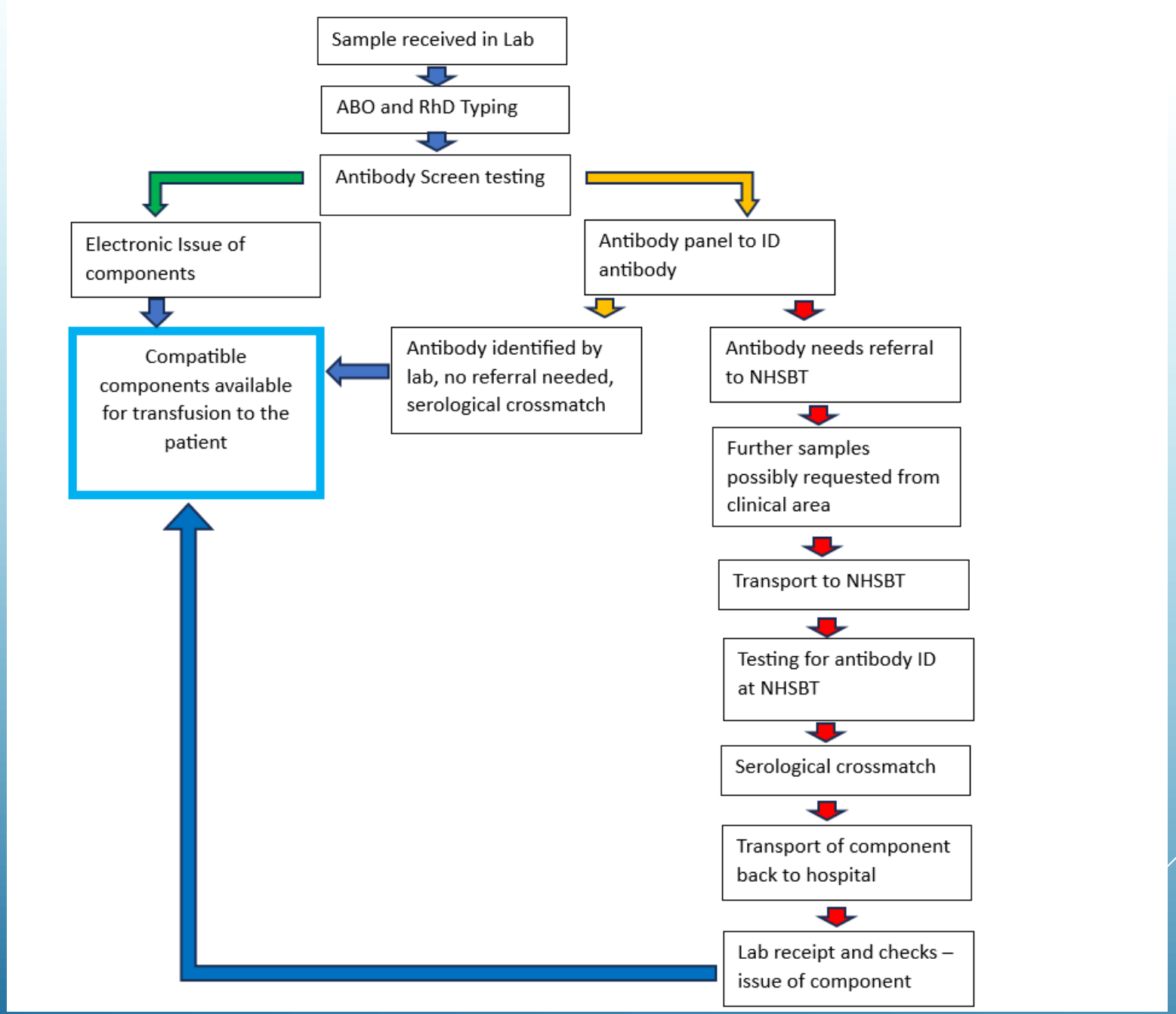


Antibody Screen

- Test patient plasma (where the antibodies are if there are any…)
- Tested against 3 reagent red cells of known types (a cocktail of red cell antigens)
- If any one is positive – further testing of panel cells is required.
- Allows ID of most antibodies …. BUT… those that are unidentifiable or need further investigation are referred to NHSBT….
- Further **communication** from the lab…

What does it mean

- Causes delay in provision of components (red cells mainly, possibly platelets* and buffy coat "anything with cells in")
- **Communication**!!! Clinical urgency vs time for testing and provision of component
- Time taken and need for referral depends on different factors, this is case specific so speak to the blood bank (specificity, referral, logistical implications of transport, testing time, location of components…. Further transport back to hospital)


Sample received in Lab
ABO and RhD Typing
Antibody Screen testing
Electronic Issue of components
Antibody panel to ID antibody
Compatible components available for transfusion to the patient
Antibody identified by lab, no referral needed, serological crossmatch
Antibody needs referral to NHSBT
Further samples possibly requested from clinical area
Transport to NHSBT
Testing for antibody ID at NHSBT
Serological crossmatch
Transport of component back to hospital
Lab receipt and checks – issue of component

General blood provision

- ABO RhD match components compatible for transfusion.
- Electronic issue in most cases, or serologically crossmatched
- Special requirements met

- Women of child bearing potential (<50yo)
  - RhD compatible
  - K- Neg blood (unless known to be K+)

Electronic Issue

- Issue of red cells for transfusion ABO/D compatible.
- LIMS system validated blood ensuring that ABO incompatible components cannot be selected/ issued.
- Patients met the following criteria:
  - Fully automated testing
  - No blood group discrepancies or anomalies
  - Antibody screen is negative

Serological crossmatch (manual)

- Suitable for all patients
- React patient plasma with proposed donor red cells for transfusion
- Confirm requirement of component selected match patient requirements, ABO/D type compatible and Antigen Neg for any known antibodies.

Clinically significant transfusion antibodies

- Not all antibodies detected are clinically significant – nuisance antibodies, no further action (N, Lea, Leb, P_1)
- Clinically significant
- Rh Anti -D, C, E, c, e,
- K – Anti-K
- JK – Anti JK^a, Anti JK^b
- MNS – Anti M, Anti S, Anti s

- For clinically significant select antigen negative units … but availability of the suitable components can vary…. **Communication** between blood bank and clinical team is necessary

Provision of specific components

- Availability of components depends on the frequency of the or prevalence of antigen neg donors.
- 91% population are K neg. therefore 9/10 units in NHSBT stock, so the blood bank will be able to easily provide, no delay
- 17% population a Fyb neg. Therefore only 1 in 5 units in the NHSBT stock, will most likely require specific request from the blood bank to NHSBT centre

- Patients with rare or multiple antibodies have a smaller pool of compatible components to select from.

Example

- Group O Pos patient – has Anti D, K, Jka, Fya
- 322 units out of 40,000 (1:125) would be suitable for this patient
- Likely need to import from another centre

Rare antibodies

- High frequency antibodies
  - <3% of population is neg for that antigen
  - These patient form an antibody and require antibody neg – increase demand on a small stock
- Different population prevalence's:
  - Caucasian population <1% Fy (a-b-)
  - Black population 66% Fy (a-b-)
- Very rare - Rh Null phenotype there are less than 50 individuals worldwide…

- **Communication** in these cases is essential, where possible forward planning in care management and information is disseminated to the relevant teams, blood bank, TP, clinical area.

Provision of components for rare cases

- National stock
- Rare donor panel
- Frozen bank
- International donor panels
- Cell salvage

Summary

- Red cell antibodies can cause destruction of transfused incompatible cells
- Identification of antibodies takes time… and can cause delays in the provision of components if not properly communicated.
- All transfusions should be risk vs. benefit.
- **Communication** must be clear between blood bank and clinical teams – provision of clinical need vs availability of compatible components
- *In emergency settings consideration must be given if concessionary releases are required for patient benefit… "Transfusion of compatible blood to a corpse is not a successful outcome of transfusion"*