

Blood Transfusion

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RBC transfusion therapy Indications

- Improve oxygen carrying capacity of blood
 - Bleeding
 - Chronic anemia that is symptomatic
 - Peri-operative management

Red blood cell transfusions

Special preparation

- CMV-negative CMV-negative patients Prevents CMV transmission
- Irradiated RBCs Immune deficient recipient Prevents GVHD
- Leukopoor Previous non-hemolytic Prevents tx reaction/CMV
- Washed RBC PNH patients Prevents hemolysis
IgA deficient recipient Prevents anaphylaxis

Categories of Transfusion Reactions

Acute

- Immunologic
 - *Hemolytic*
 - *Febrile*
 - *Allergic*
 - Anaphylactic
 - *TRALI*

- Non-immunologic
 - *Circulatory Overload*
 - Hemolytic
 - Physical
 - Bacterial contamination
 - Air embolus
 - Metabolic reaction

Categories of Transfusion Reactions

Delayed (> 24 hours)

- Immunologic
 - Alloimmunization
 - RBC
 - HLA
- Hemolytic
- GVHD
- Post-transfusion
Purpura
- Immunomodulation
- Non-immunologic
 - Iron overload
 - ***Viral infections***
 - HCV
 - HBV
 - HIV
 - HTLV
 - Other organisms
 - Malaria, Chagas,
Babesiosis, etc

Protocol for ALL acute transfusion reactions

- STOP THE TRANSFUSION immediately
- Maintain IV access with 0.9% NaCl
- Check blood component for patient ID
- Notify Blood Bank(BB)
- Send blood sample and urine to BB
- Keep blood unit in case culture becomes necessary
- Support patient as necessary

Transfusion-transmitted disease

Infectious agent	Risk
HIV	~1/4 million
Hepatitis C	1/ 1.4 million
Hepatitis B	1/ 3 million
Hepatitis A	<1/1,000,000
HTLV I/II	1/640,000
CMV	50% donors are sero-positive
Bacteria	1/250 in platelet transfusions
<u>Creutzfeld-Jakob disease</u>	Unknown
Others	Unknown

Platelet transfusions

- Platelet concentrate (Random donor)
- Pheresis platelets (Single donor)

- Target level
- Bone marrow suppressed patient
- ($>10-20,000/\mu\text{l}$)
- Bleeding/surgical patient
- ($>50,000/\mu\text{l}$)



Platelet transfusions - complications

- Higher incidence than in RBC transfusions
- Related to length of storage/leukocytes/RBC mismatch
- Bacterial contamination
- Platelet transfusion refractoriness
 - Alloimmune destruction of platelets (HLA antigens)
 - Non-immune refractoriness
 - Microangiopathic hemolytic anemia
 - Coagulopathy
 - Splenic sequestration
 - Fever and infection
 - Medications (Amphotericin, vancomycin, ATG, Interferons)

Fresh frozen plasma

- Indications
 - Multiple coagulation deficiencies (liver disease, trauma)
 - DIC
 - Warfarin reversal
 - Coagulation deficiency (factor XI or VII)
- Dose (225 ml/unit)
 - 10-15 ml/kg
- Note
 - Viral screened product
 - ABO compatible

Vocabulary

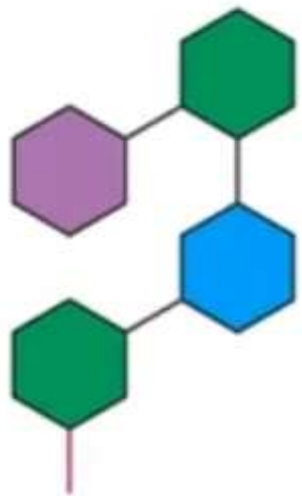
- **Gene:** The basic physical unit of heredity
-An individual has 2 genes for every trait (one from father, one from mother)
- **Phenotype:** The observable traits of an organism
- **Genotype:** Genetic makeup of an organism
- **Allele:** One member of a pair of genes that occupies a certain space in the genome (locus)
- **LOCUS:** A space in the genome occupied by an allele
- **Homozygous:** Having 2 of the same alleles
- **Heterozygous:** Having 2 different forms of an allele

Blood Group System

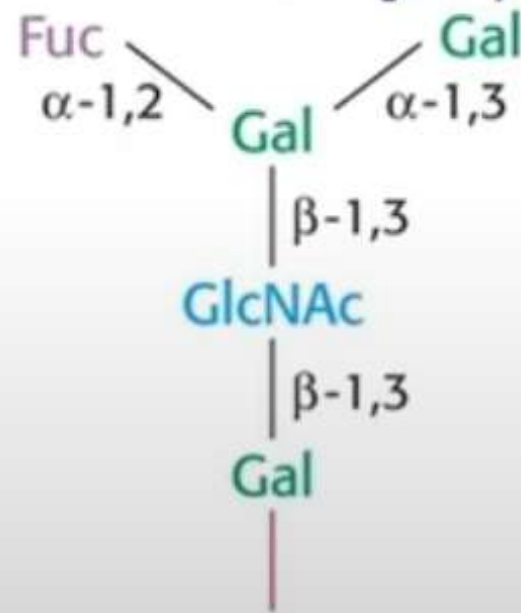
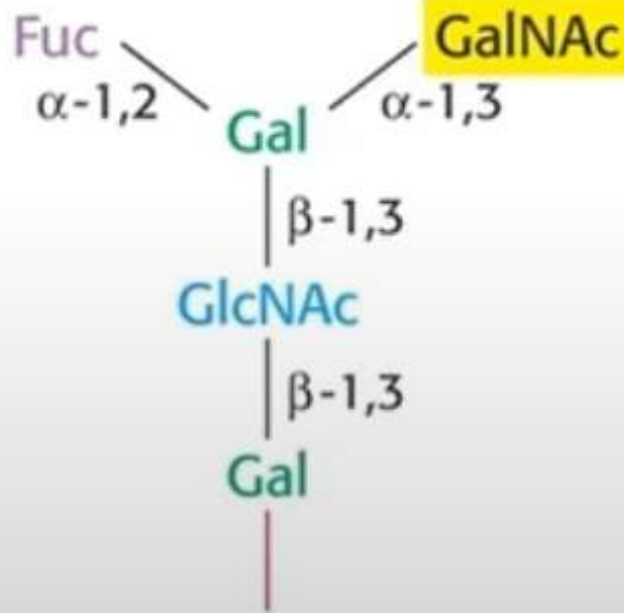
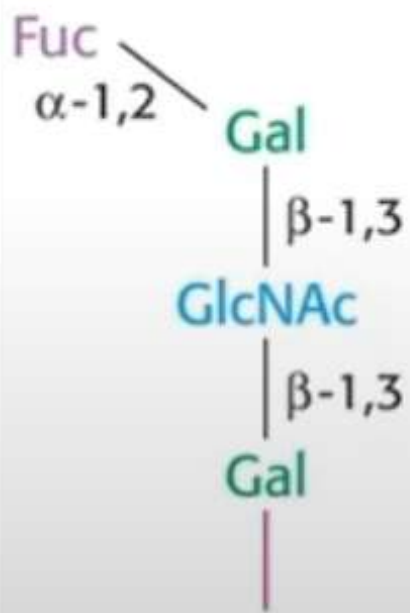
**A set of variant antigens
resulting from alleles of a single locus,

each defining a common serological
phenotype.**

A, B, & O oligosaccharide antigens (blood groups)



Specific glycosyltransferases add group to O antigen



O antigen

A antigen

B antigen

Foundation oligo (frameshift mutant gene), one from each parent

ABO blood types

Blood type	Antigens on RBCs	Serum antibodies
A	A	Anti-B
B	B	Anti-A
AB	A and B	Neither
O	Neither	Anti-A and anti-B

- The antibodies are induced by exposure to cross-reacting microbial antigens present on common intestine bacteria.
- ABO blood-group antigens have subtle differences in the terminal residues of the sugars on glyco-proteins in RBC.
- Providing the basis for blood typing test in blood transfusion

Summary: 38 blood group systems, 45 genes

Also detailed: non-human counterparts for H/h, MN, Rh

System	Locus	Function	Alleles	System	Locus	Function	Alleles
ABO	<u>ABO</u>	enzyme	115	Landsteiner-Weiner	ICAM4 (LW)	adhesion	3
<u>Chido- Rodgers</u>	C4A, C4B	factor	7+	Lewis	FUT3, FUT6, FUT7	enzymes	36
Colton	AQP1	channel	7				
Cromer	DAF	receptor	13				
Diego	SLC4A1	exchanger	78	Lutheran	LU	adhesion	16
<u>Dombrock DO</u>	unknown		9	MNS	GYPA, GYPB, GYPE	unknown	43
Duffy	FY	receptor	7				
<u>Gerbich (Ge)</u>	GYPC	structure	9				
GIL	AQP3	channel	2	OK	BSG	adhesion	5
H/h	FUT1, FUT2	enzymes	57	P-related	A4GALT, B3GALT3	enzymes	27
I	GCN2 (IGnT)	enzyme	8	RAPH-MER2	CD151		3
Indian (IN) CD44	adhesion		2	Rh	RHCE, RHD, RHCG	transport	126
JMH	SEMA7A	signaling	0		RHAG, RHBG		
<u>Kell (with Kx)</u>	KEL, XK	enzyme	67	<u>Scianna Xg</u>	ERMAP	adhesion	4
Kidd	SLC14A1	transport	8		XG, CD99 (MIC2)	adhesion	0
Knops	CR1	receptor	24+	YT	ACHE	enzyme	4

20th Century Transfusions

1902

AB Group discovered

1907

Importance of crossmatching blood between donor & recipient

1914

Sodium Citrate proposed as anticoagulant

1936

First Blood Bank: Barcelona, Spanish Civil War

1940

Levine & Landsteiner, Rhesus blood Group System

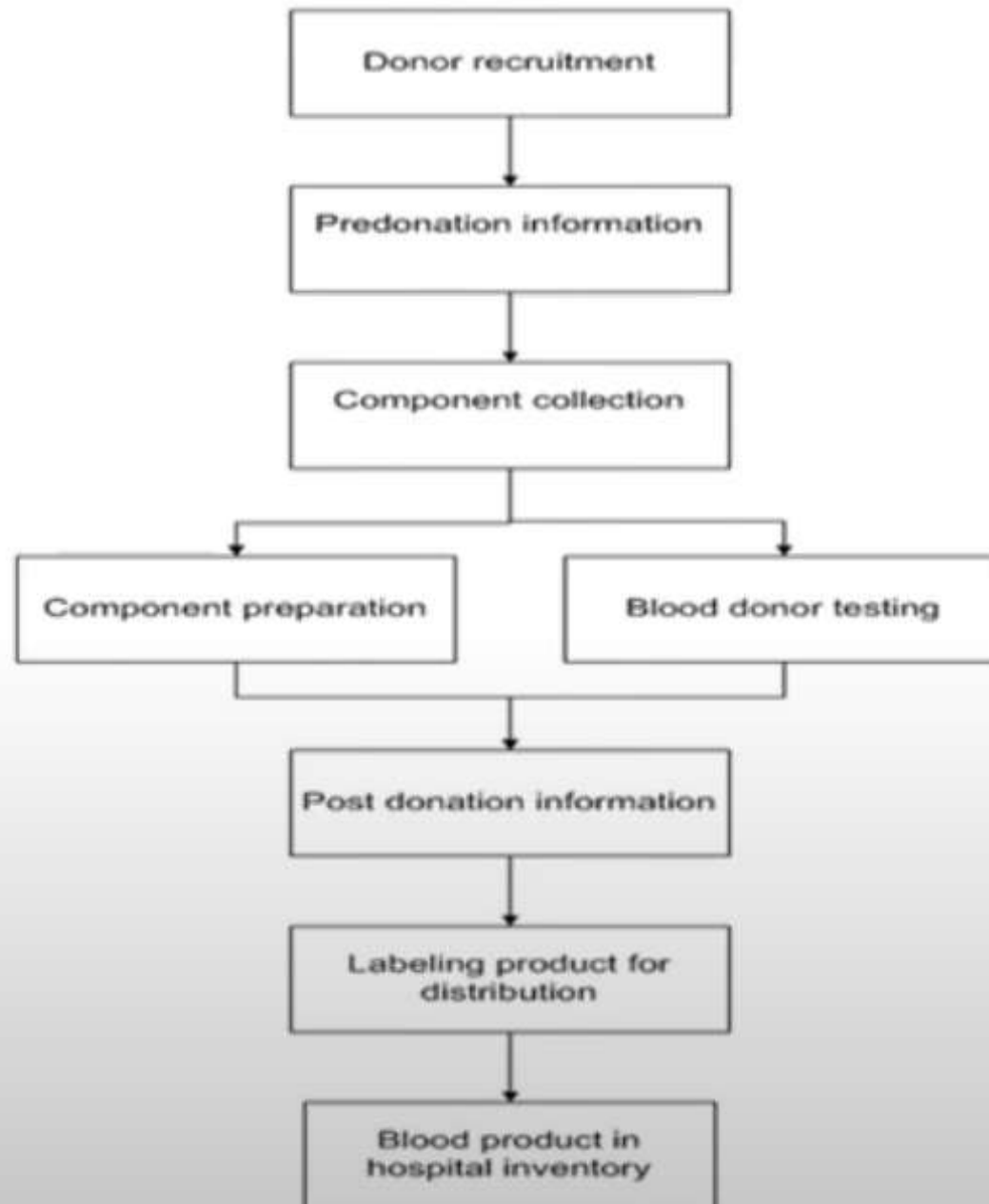
Aims of Transfusion Centre

- Provision of Blood of the best possible quality and safety for the patient receiving it
- To care for the donor - ensure act of donation does not harm donor

Blood Supply Chain

- Blood Donor Screening Criteria
- Donation Process
- Donation Testing
- Component preparation
- Plasma Products

Blood Donation Process



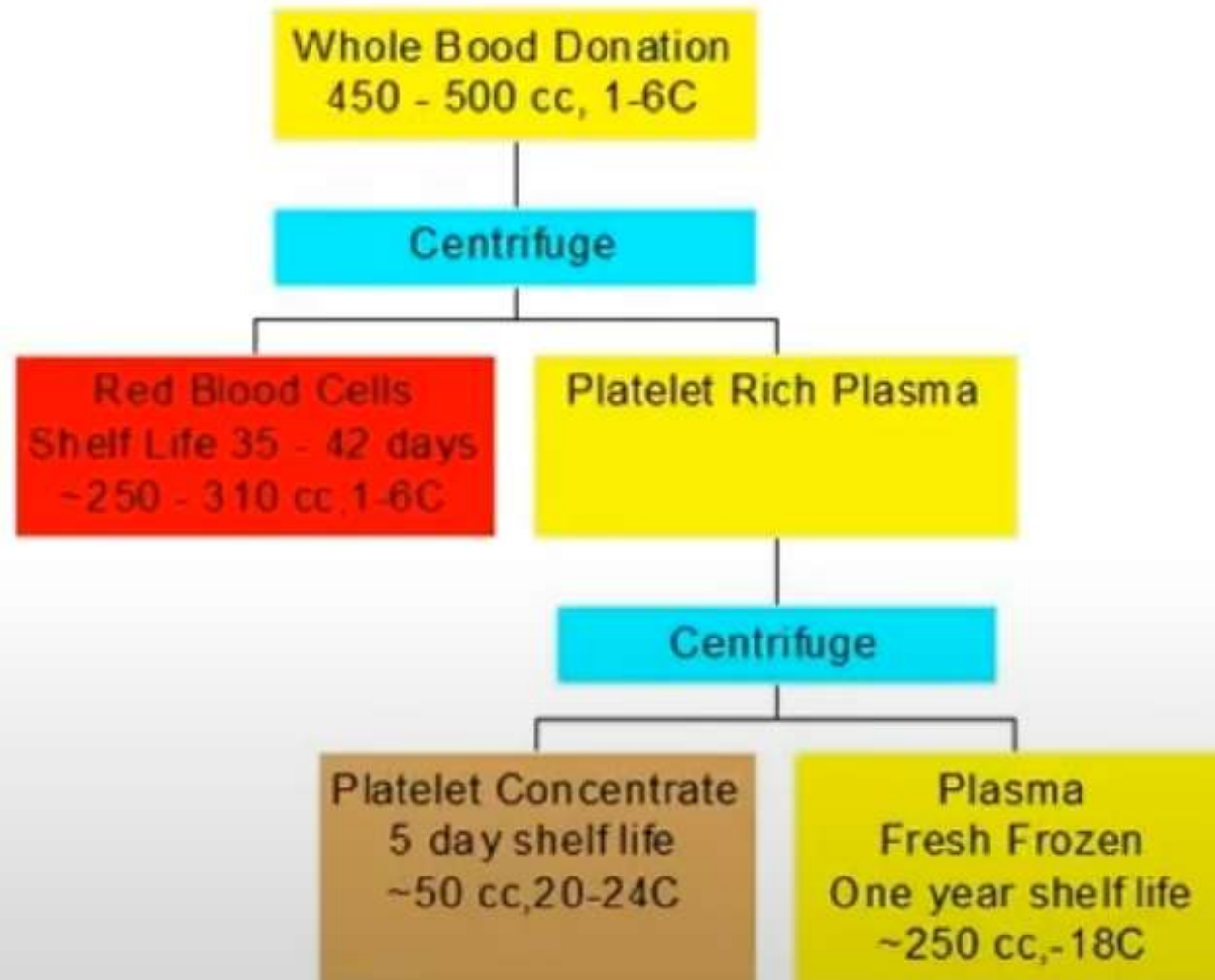
Blood Donor Criteria

- Age 17-65 (new donors until 60)
- Weight > 50kg
- General health
- Specific illnesses
- Contact with infection

Blood Donation

- 475mls Blood + 63mls anticoagulant
 - Red Cells
 - Plasma
 - Buffy Coat → Platelets
- Red Cells + Optimal Additive Solution
 - Saline
 - Adenine
 - Glucose
 - Mannitol
- Expiry date 35 days

Blood Collection and Manufacturing



Plasma/Red Cell Separation

Centrifugation



Plasma expression



Leucodepletion

- Universal leucodepletion introduced in 1999 to reduce the risk of vCJD transmission by blood
- other benefits - less febrile reactions, less alloimmunisation, less GVHD, ? reduce immunosuppressive effects
- Less CMV

Blood Donation Testing

- Microbiology markers
- Blood grouping and screening for high titre antibodies
- Quality monitoring

Transfusion Related Acute Lung Injury - TRALI

- Not rare but under diagnosed
- A potentially fatal condition
- Presents as pulmonary oedema
- Occurs within 1-4 hrs of starting transfusion

Clinical Features

- Acute respiratory distress
- Fever with chills
- Non productive cough
- Cyanosis
- Hypotension
- Chest pain
- Bilateral pulmonary oedema
- Chest X ray – bilateral pulmonary infiltrates in
hilar region

CXR in TRALI



Bilateral pulmonary infiltrates
in hilar region



Physiologic/Radiographic Features

- $\text{PaO}_2/\text{FiO}_2 < 300$ ALI, < 200 ARDS
- Bilateral infiltrates consistent with pulmonary edema.
- No clinical evidence of left atrial hypertension, $\text{Pawp} < 18$ mm Hg.
- \downarrow Lung compliance / \uparrow Airway pressure
- Positive pressure ventilation via endotracheal tube.

Classical Theory (Immune TRALI)

- Donor antibodies react with patient neutrophils
- Neutrophils sequester in pulmonary vasculature
- Complement and cytokines liberated
- Damage to endothelium
- Results in pulmonary oedema

Two Hit Theory (Non-immune TRALI)

Predisposing Conditions:^I

- Sepsis
- Surgery
- Haematological malignancies
- Trauma

Pulmonary endothelial activation and neutrophil sequestration

Lipids and WBC antibodies activate neutrophils which then causes endothelial damage

Management - TRALI

- No specific treatment
- Largely supportive
- Respiratory support with O₂
- Most cases require mechanical ventilation
- Steroids
- Clinical staff who administer transfusions must be aware how to diagnose & manage promptly

Implicated Donors and Prevention

- Implicated donors are usually “multipara” female due to exposure to paternal leucocyte antigens from the fetus during pregnancy.
- The percentage of women with antibodies increases with increasing number of pregnancies.