

# Blood Transfusion/MS4

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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  
IgA deficient recipient    Prevents hemolysis  
Prevents anaphylaxis

# Categories of Transfusion Reactions

## Acute

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- 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)

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- 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

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- 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	~1/500,000
• Hepatitis C	1/600,000
• Hepatitis B	1/500,000
• Hepatitis A	<1/1,000,000
• HTLV I/II	1/640,000
• CMV	50% donors are sero-positive
• Bacteria	1/250 in platelet transfusions
• Creutzfeld-Jakob disease	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

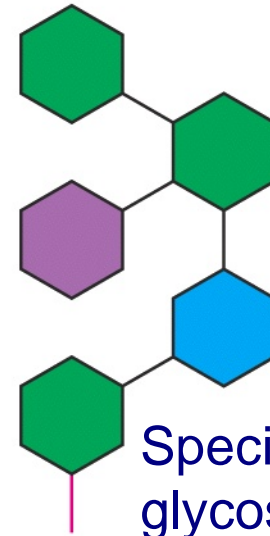
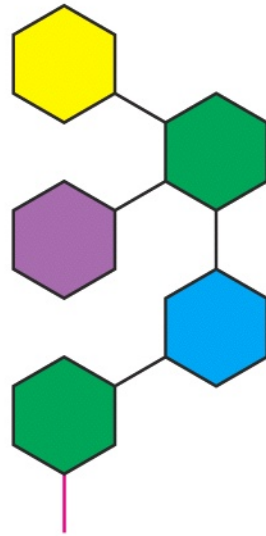
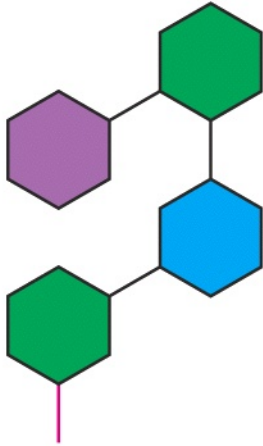
# Vocabulary

- **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

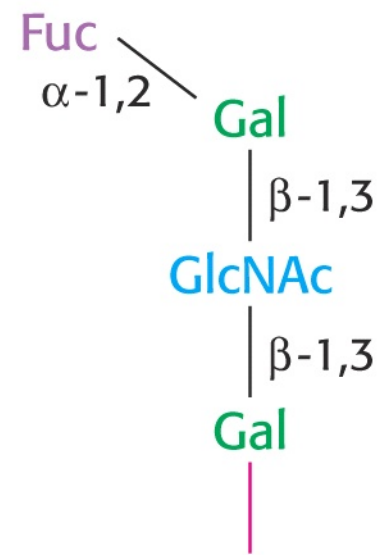
## Blood Group System

**A set of variant antigens  
resulting from alleles of a single locus,  
  
each defining a common serological  
phenotype.**

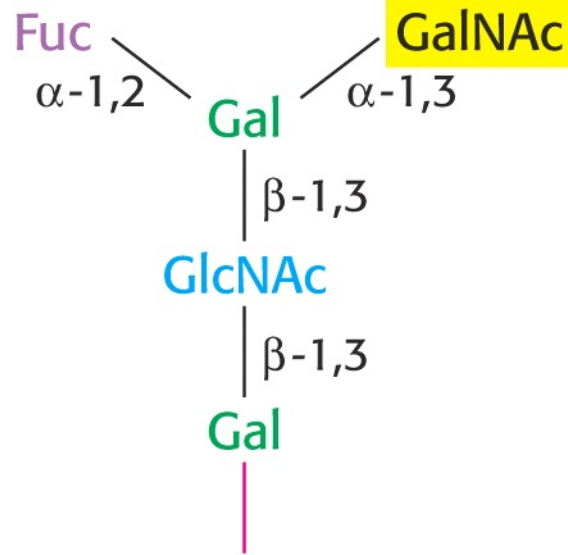
# A, B, & O oligosaccharide antigens (blood groups)



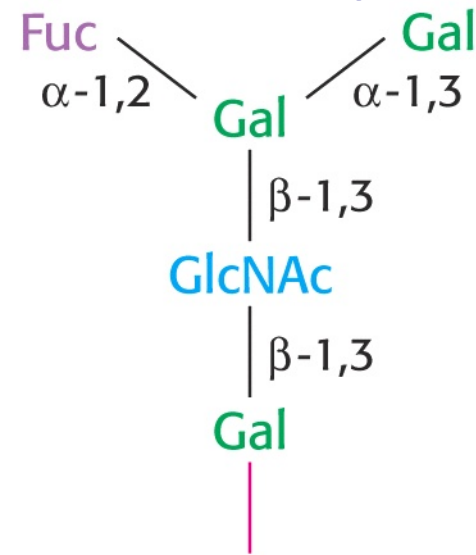
Specific glycosyltransferases add group to O antigen



**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: 29 blood group systems, 40 genes, 707 alleles

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

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

# 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

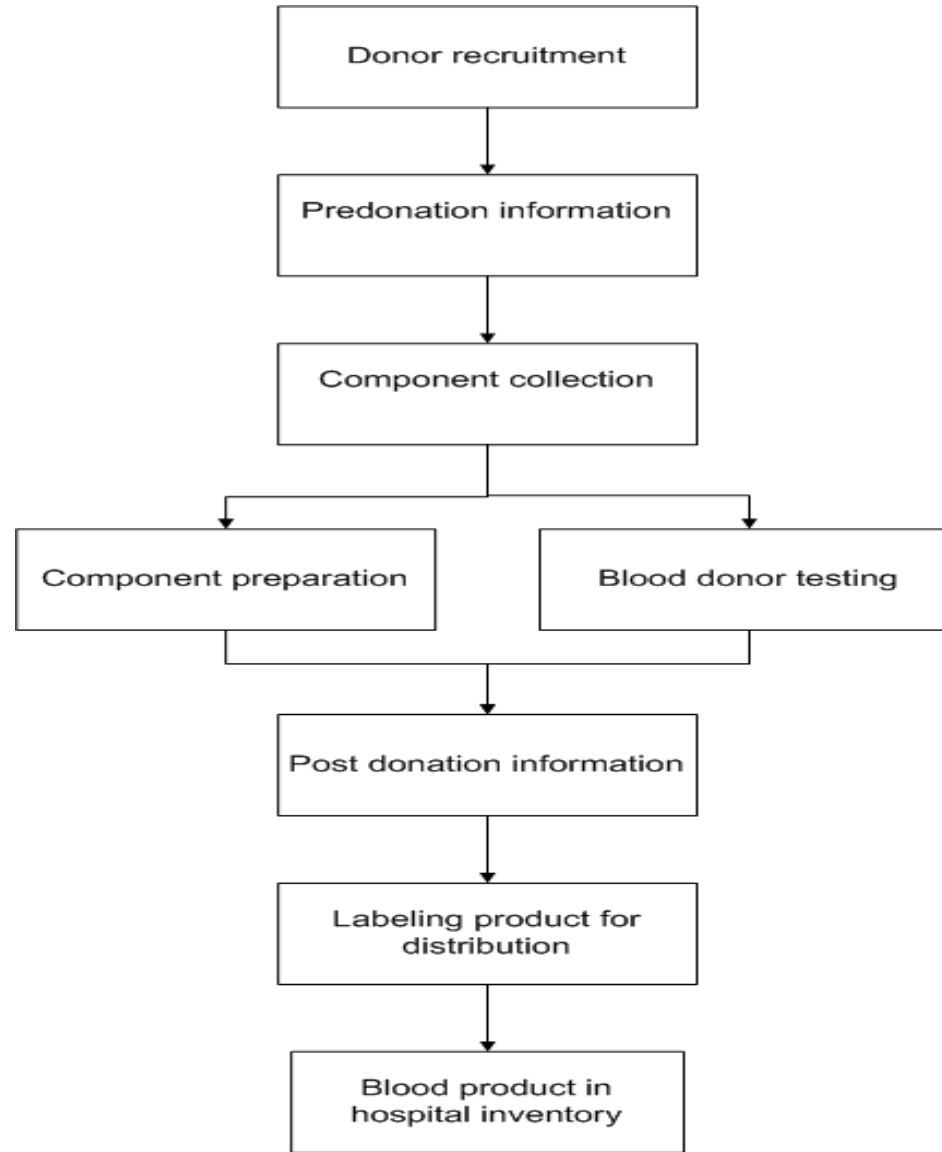
- Provision of Blood of the best possible quality and safety for the patient receiving it
- To care for the donor - ensure act of donation does not harm donor

# Blood Supply Chain

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

# Blood Donation Process

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# Blood Donor Criteria

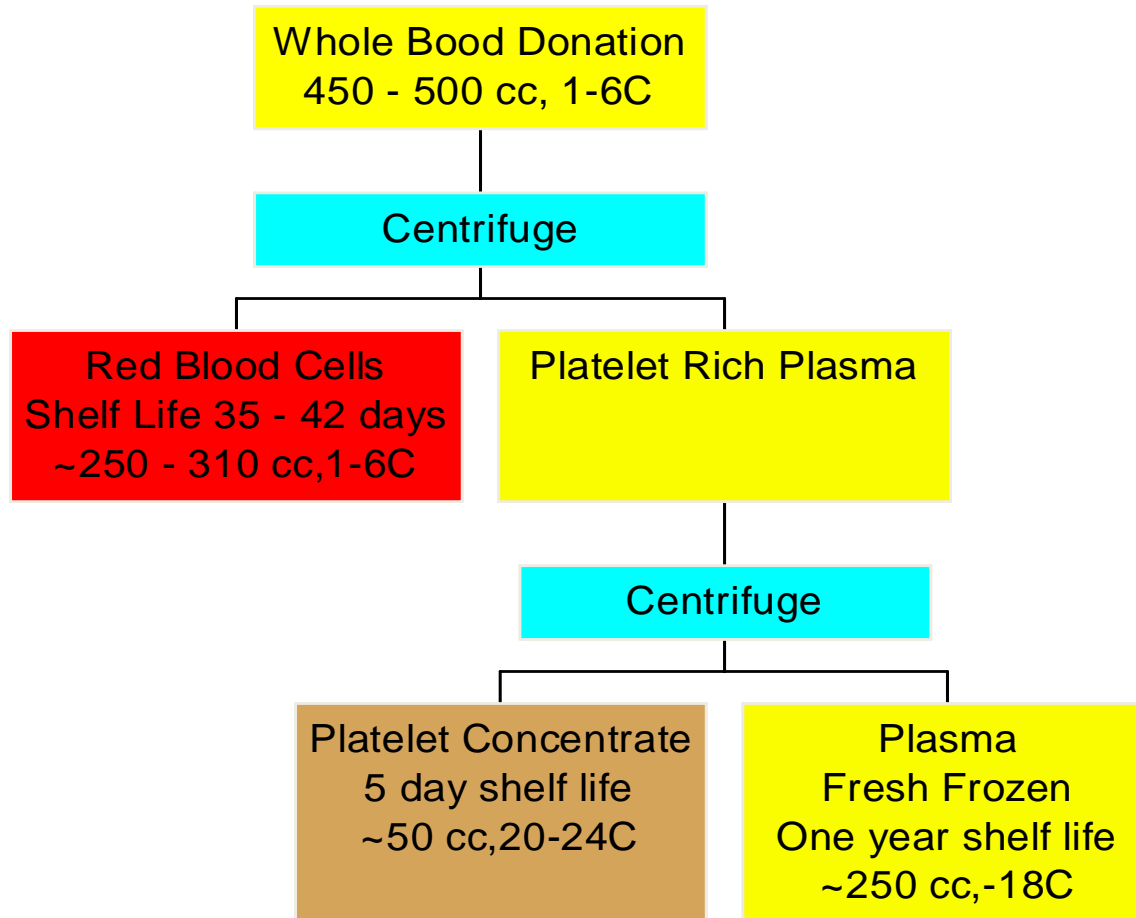
- Age 17-65 (new donors until 60)
- Weight > 50kg
- General health
- Specific illnesses
- Contact with infection

# 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

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# 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

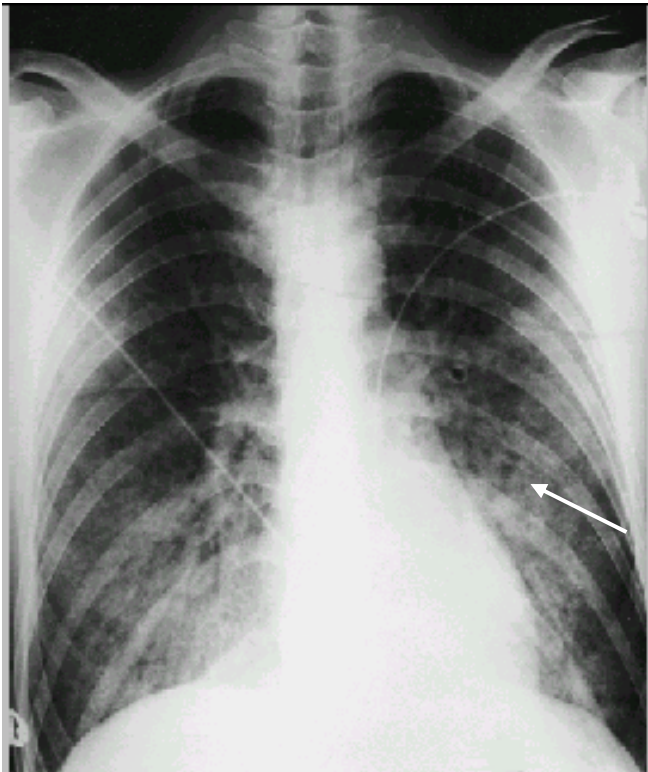
# Transfusion Related Acute Lung Injury - TRALI

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

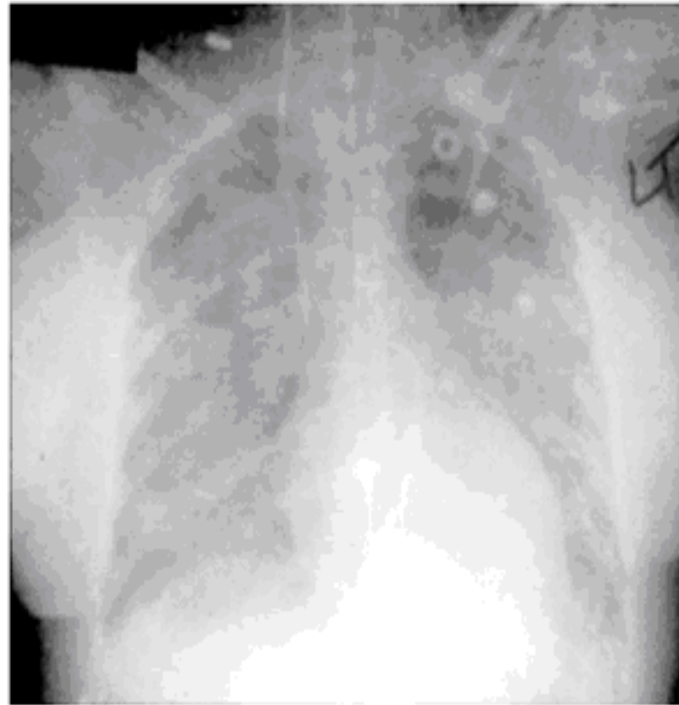
# Clinical Features

- 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:

- 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 O<sub>2</sub>
- 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.