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

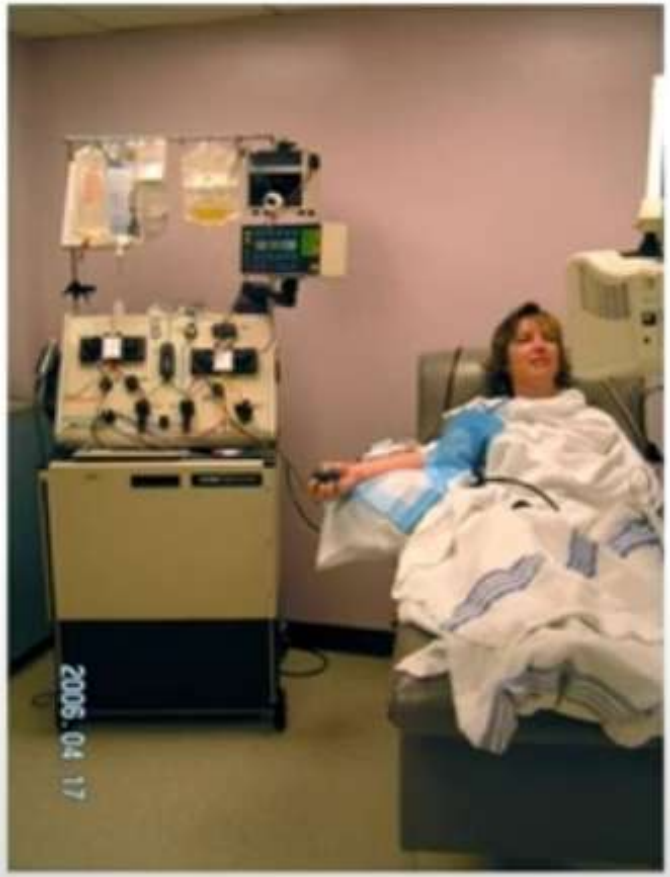
Transfusion-transmitted disease

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
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/µl)
- Bleeding/surgical patient
- (>50,000/µl)



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)

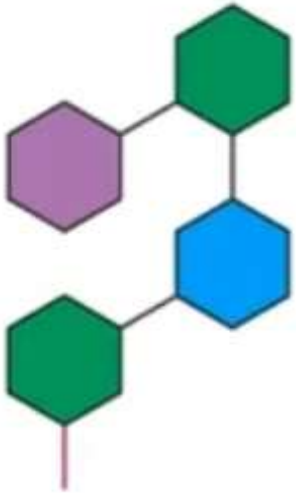
- **Phenotype:** The observable traits of an organism
- **Genotype:** Genetic makeup of an organism
- **Allele:** One member of a pair of genes that occupies a certain space in the genome (locus)
- LOCUS: A space in the genome occupied by an allele
- **Homozygous:** Having 2 of the same alleles
- **Heterozygous:** Having 2 different forms of an allele

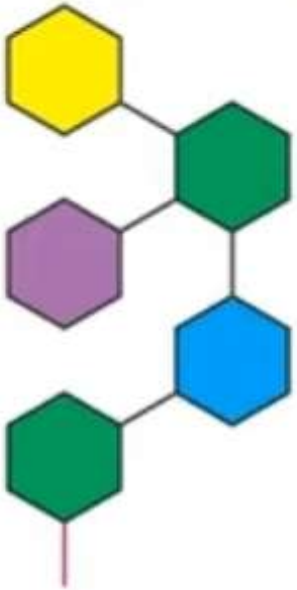
Blood Group System

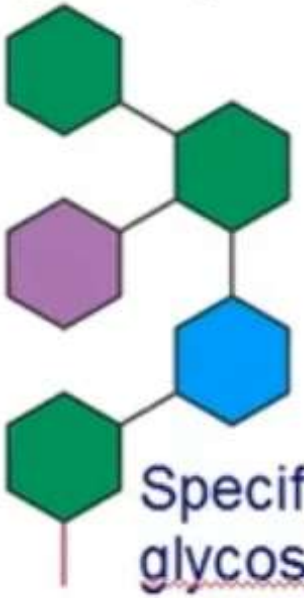
A set of variant antigens
resulting from alleles of a single locus,

each defining a common serological phenotype.

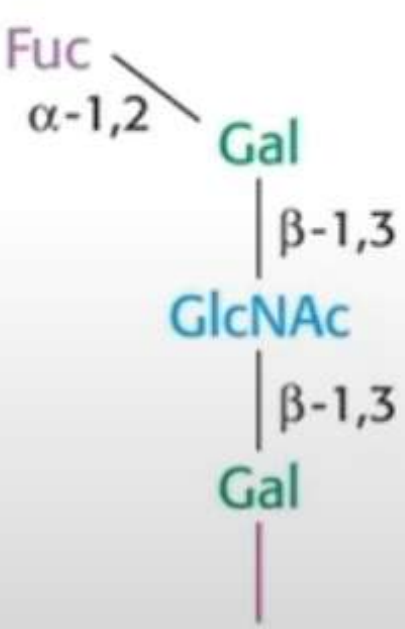
A, B, & O oligosaccharide antigens (blood groups)



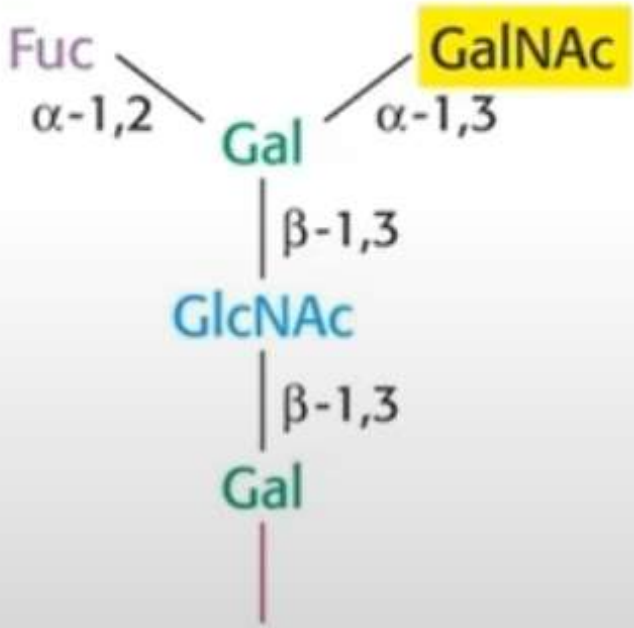




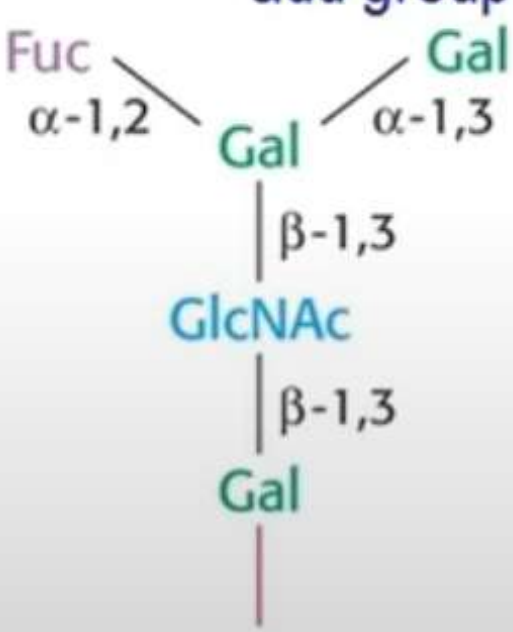
Specific glycosyltransferases add group to O antigen



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	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				
Cromer	DAF	receptor	13				
Diego	SLC4A1	exchanger	78	Lutheran	LU	adhesion	16
Dombrock DO	unknown	9		MNS	GYPA, GYPB, GYPE	unknown	43
Duffy	FY	receptor	7				
Gerbich (Ge)	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
				Rh	RHCE, RHD, RHCG RHAG, RHBG	transport	126
Indian (IN) CD44	adhesion	2					
JMH	SEMA7A	signaling	0				
Kell (with Kx)	KEL, XK	enzyme	67	Scianna	ERMAP	adhesion	4
				Xg	XG, CD99 (MIC2)	adhesion	0
Kidd	SLC14A1	transport	8				
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

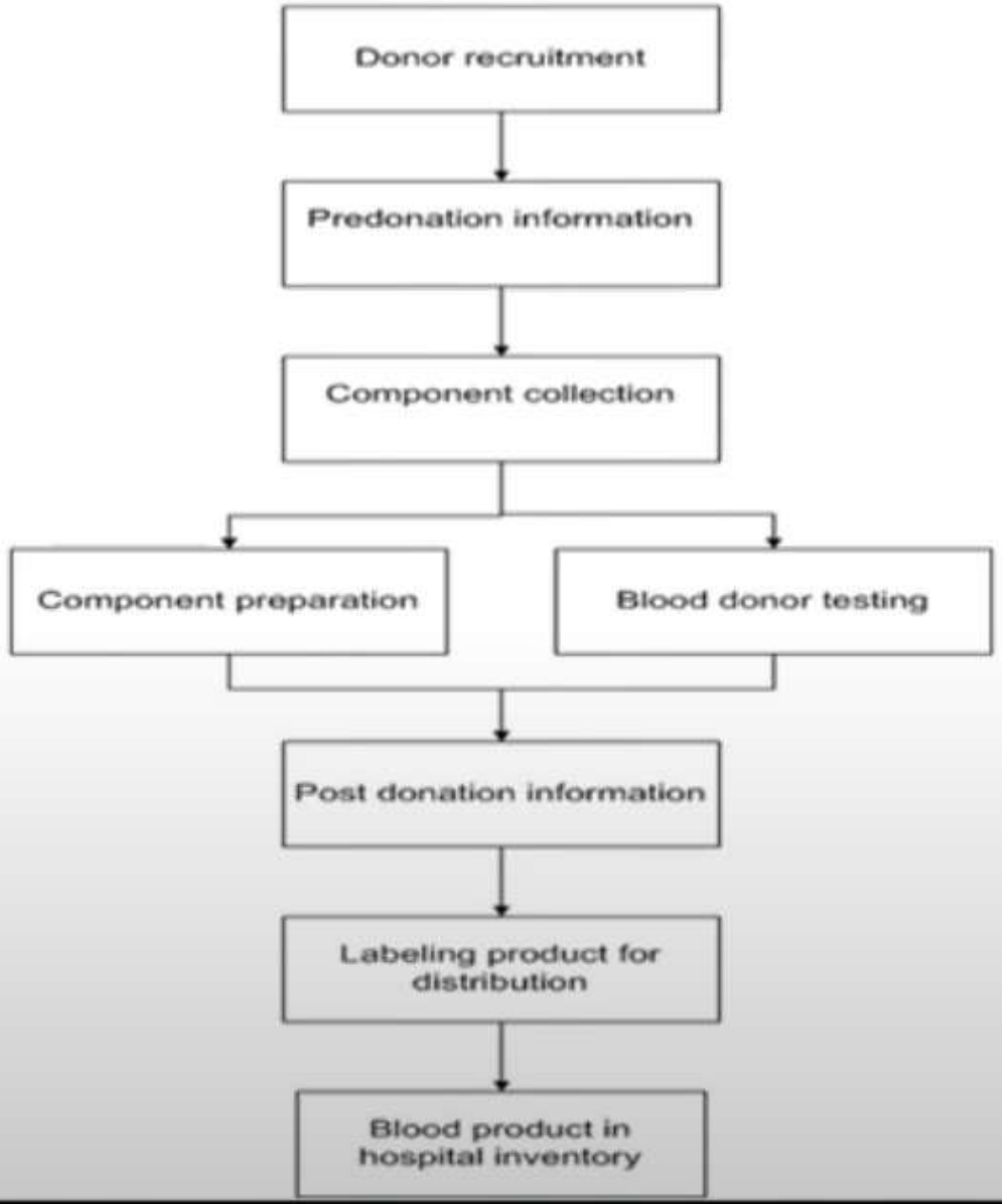
- Provision of Blood of the best possible quality and safety for the patient receiving it

- 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



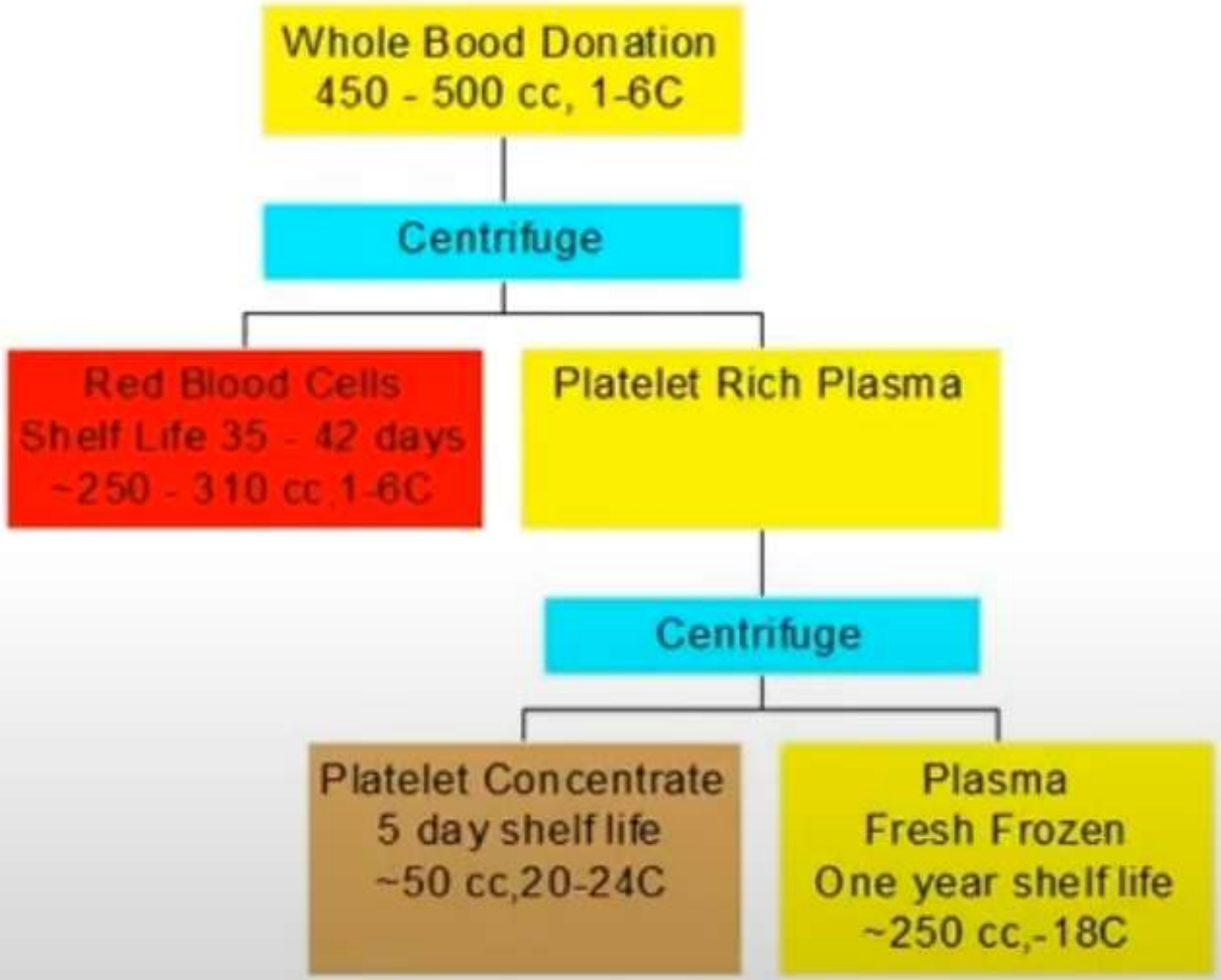
Blood Donor Criteria

- 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 immunosuppresssive effects
- Less CMV

Blood Donation Testing

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

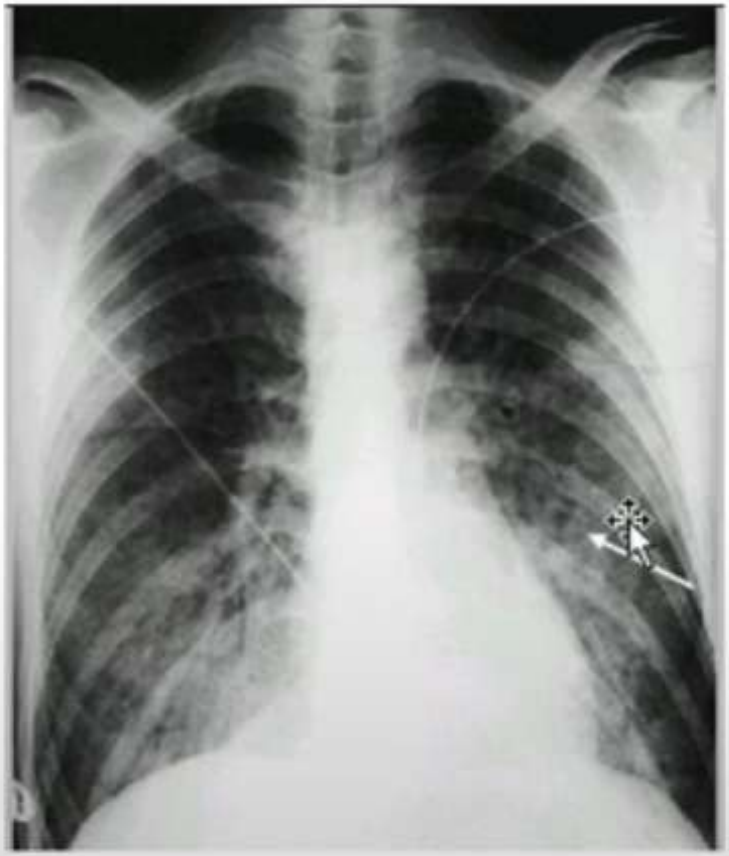
Transfusion Related Acute Lung Injury - TRALI

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

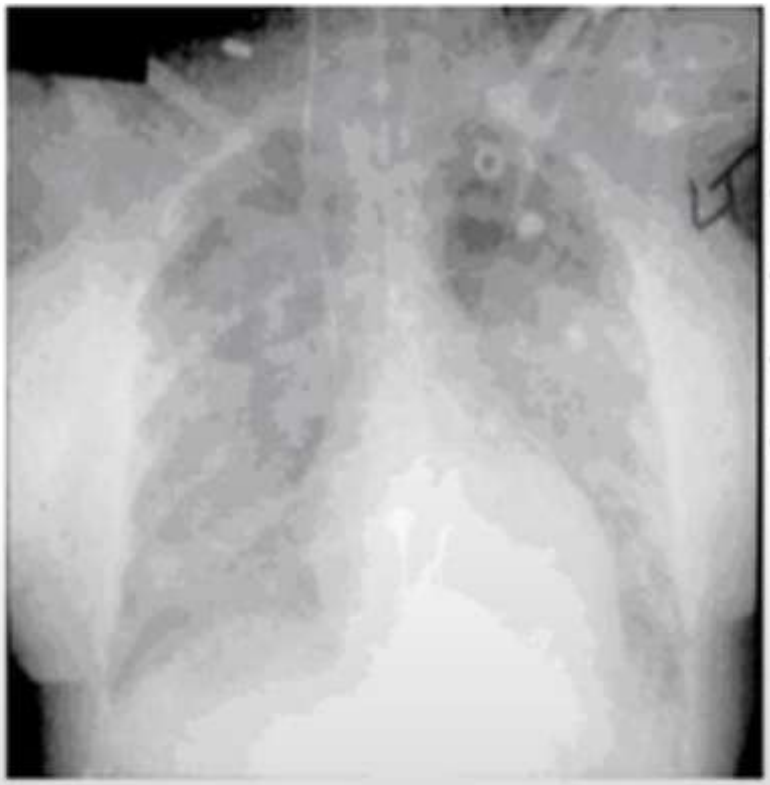
Clinical Features

- 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

- PaO_2/FiO_2 < 300 ALI, < 200 ARDS
- Bilateral infiltrates consistent with pulmonary edema.
- No clinical evidence of left atrial hypertension, Pawp < 18 mm Hg.
- ↓ Lung compliance / ↑ Airway pressure
- Positive pressure ventilation via endothracheal tube.

Classical Theory
(Immune TRALI)

- Donor antibodies react with patient neutrophils
- Neutrophils sequestrate 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_2
- 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.