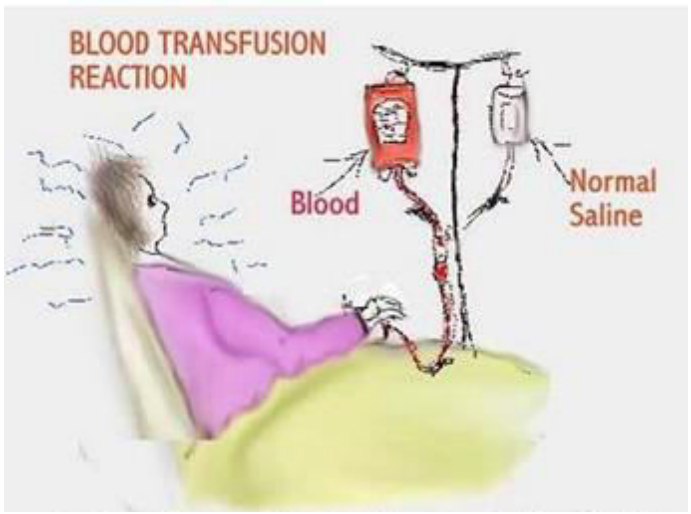
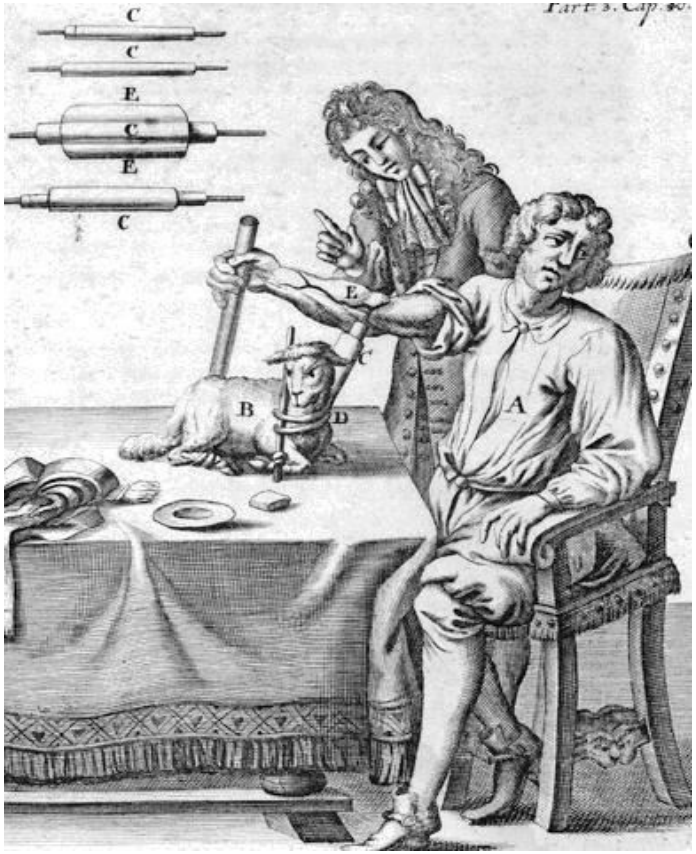


Transfusion Reactions & Management

BY
Dr.A.Yashovardhan
Assistant Professor
Dept. of Transfusion Medicine
NMCH

History



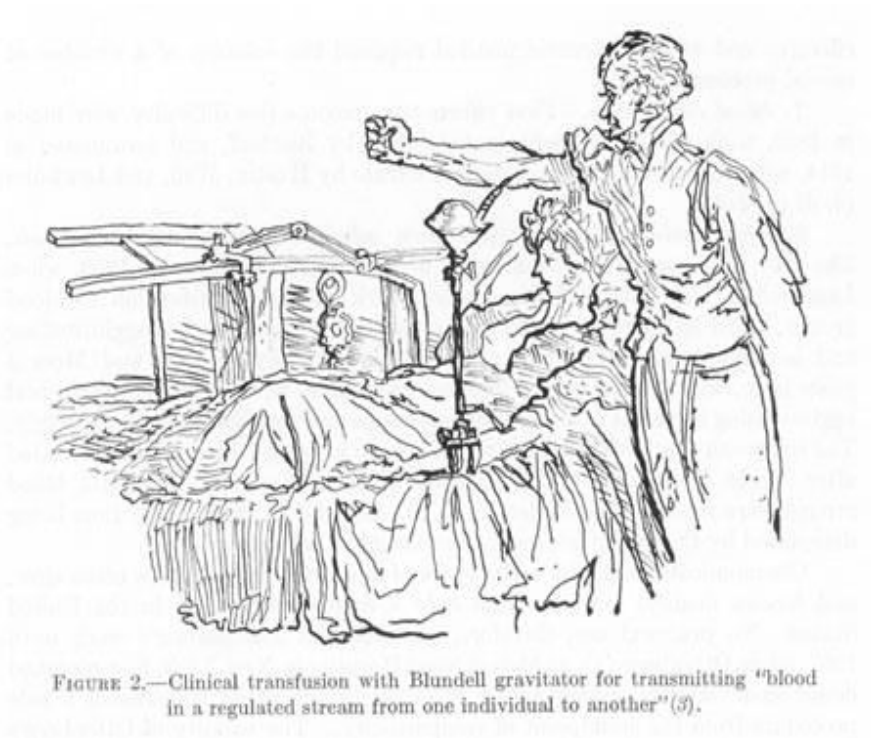
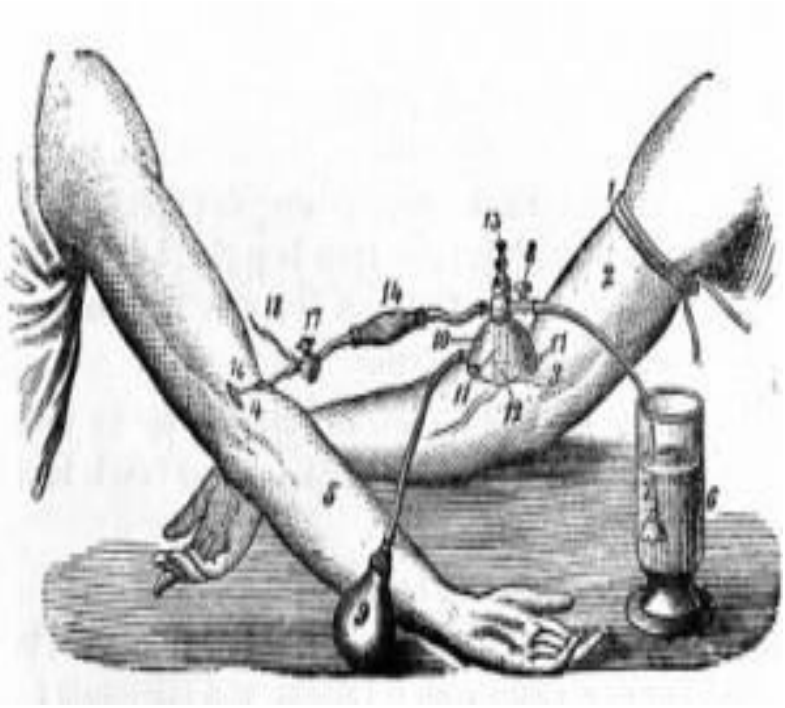


FIGURE 2.—Clinical transfusion with Blundell gravitator for transmitting "blood in a regulated stream from one individual to another"(3).



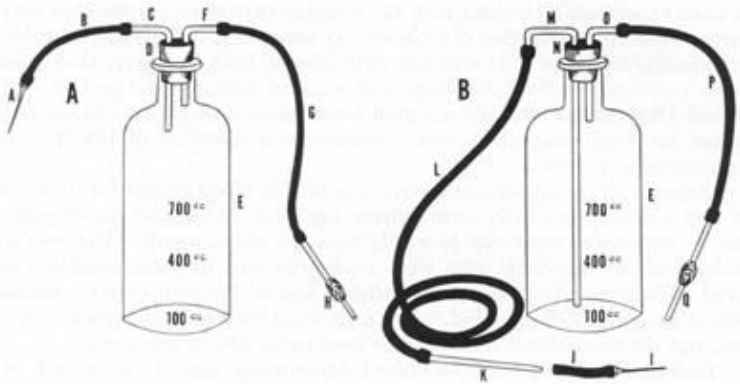


FIGURE 3.—Blood transfusion apparatus used in World War I.

A. a. Transfusion needle.
b. Rubber tube.
c. Glass tube.
d. Rubber stopper.
e. 1-liter bottle.
f. Glass tube.
g. Rubber tube.
h. Glass tube for suction, with cotton in bulb.

B. i. Transfusion needle.
j. Rubber tube.
k. Glass tube.
l. Rubber tube.
m. Glass tube.
n. Rubber stopper.
o. Glass tube.
p. Rubber tube.
q. Glass tube for exerting compression (cotton in bulb) (*27*).

Transfusion Reaction – History

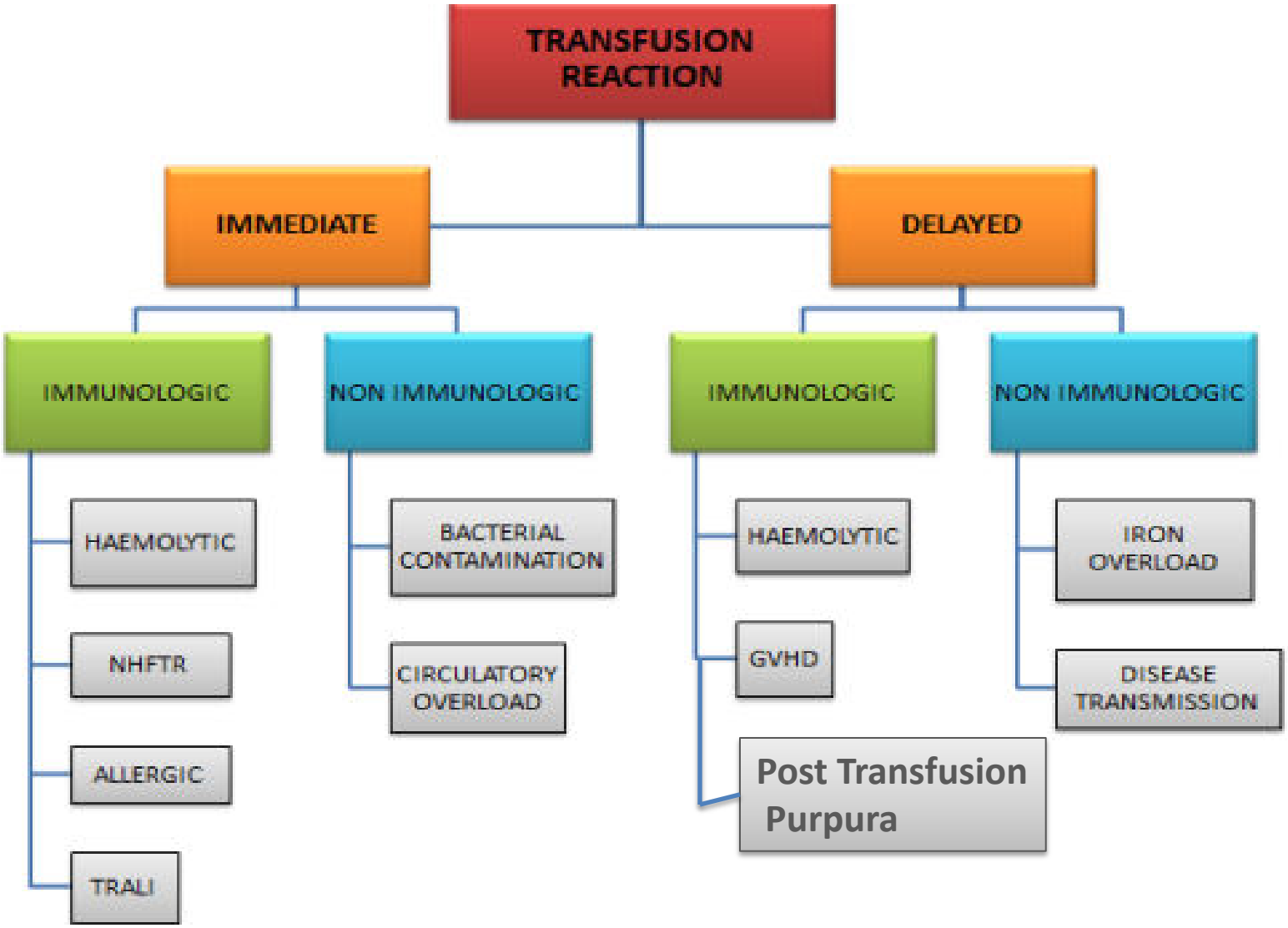
- 1492 – to save life of Pope Innocent VIII received blood of three young boys – finally all were dead.

- 1667 – Denis – transfused four subjects with animal blood (less full of impurities)
  - First two subjects not affected adversely
  - Pt. Anthony du Mauroy 34 years – suffered from intermittent bouts of maniacal behavior.
  - On 19th December 1667, removed 10 ounces of mans blood and replaced with 5 or 6 ounces of blood from the femoral artery calf
  - Pt. experiences sudden increase in pulse, plentiful sweats over face, complained of great pains in kidneys
  - Pt. passes black color urine next day morning
  - Transfusion tried in that patient again and patient finally dies

Transfusion Reaction

- Any adverse effect or unfavorable consequence occur during or after transfusion

- Types
  - Acute – with in 24 hours
  - Delayed – after 24 hours
  - Immunological
  - Non-immunological

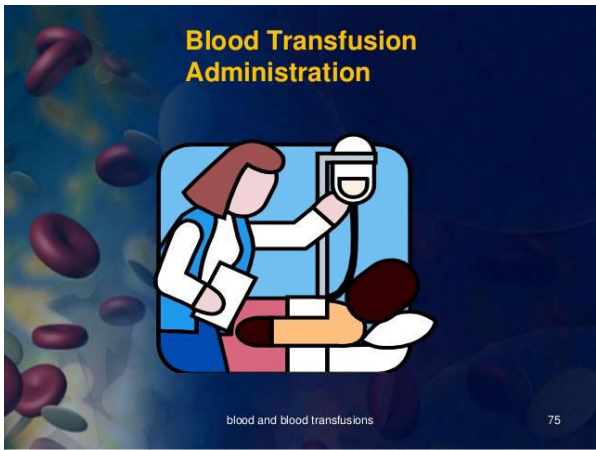

TRANSFUSION REACTION
IMMEDIATE
DELAYED
IMMUNOLOGIC
NON IMMUNOLOGIC
IMMUNOLOGIC
NON IMMUNOLOGIC
HAEMOLYTIC
NHFTR
ALLERGIC
TRALI
BACTERIAL CONTAMINATION
CIRCULATORY OVERLOAD
HAEMOLYTIC
GVHD
Post Transfusion Purpura
IRON OVERLOAD
DISEASE TRANSMISSION

Acute Hemolytic Transfusion Reaction

- Accelerated Clearance or lysis of transfused red cells due to immunological incompatibility.

- Etiology :
  - Majority of reactions due to incompatible red cell transfusions
    - Clerical errors
    - Technical errors
  - Few reported during FFP and Platelet transfusion (contamination with red cells)

- Occurs with in minutes after transfusion



- Pathophysiology:
  - Interaction of antigen and antibody
  - IgM antibody & compliment activation
  - Cytokine production (TNF ά, IL – 6 etc)
  - Histamine and serotonin secretion

- Signs and Symptoms:
  - Fever, chills, facial flushing, chest pain, Back or Flank pain, Hypotension, abdominal pain, dyspnea, vomiting
  - Hemoglobinuria, hemoglobinemia, shock, anemia, oliguria or anuria, Disseminated intravascular coagulation.
  - In anesthetized patients – diffuse oozing from surgical site, hypotension, hemoglobinuria

Management

Stop Transfusion

Table 52-6. Therapeutic Options in Hemolytic Transfusion Reactions

Therapeutic Intervention	Indication	Typical Dose
Hydration	• Prevent renal impairment • Maintain urine output >100 mL/hour	• Normal saline and/or 5% dextrose 200 mL/m^2/hour
Alkalinization of urine	• Prevent renal impairment • Maintain urine pH >7.5	• NaH_2CO_3 40 to 70 mEq in 1 liter 5% dextrose
Diuresis	• Prevent renal impairment	• Mannitol 20% 100 mL/m^2* • Furosemide 40 to 80 mg
Vasodilation	• Increase renal blood flow	• Dopamine 1 to 5 μg/kg/minute
Anticoagulation	• Treat intravascular coagulation	• Heparin 5 to 10 units/kg/hour, 0.15 to 0.25 unit per mL
Red cell exchange transfusion	• Decrease load of incompatible red cells	• Exchange of one estimated red cell mass
Plasma or platelet transfusion	• Treat hemorrhagic complications of disseminated intravascular coagulation	• Platelets: 1 unit Platelets/10 kg (max. 6 units) or 1 unit Apheresis Platelets • Plasma: 10 mL/kg Fresh Frozen Plasma
Intravenous immunoglobulin	• Prevent extravascular hemolysis†	• 400 mg/kg

*Ensure adequate renal function to prevent fluid overload from increased intravascular volume.
†Investigational. Not standard therapy.

Febrile Non hemolytic Transfusion Reaction (FNHTR)

- Increase in body temperature of 1^{o}C or more that occurs during or within several hours of transfusion and is unrelated to hemolysis, sepsis or other known cause of fever.

- The fever of FNHTR usually persists no more than 8 to 12 hours after the start of transfusion. If fever persists 18 to 24 hours or longer, it is unlikely to be transfusion related. Generally, FNHTRs are self-limited and have no sequelae.

- Transfusion of cellular blood products (leukocytes & cytokines) implicated for FNHTR.

- Signs & Symptoms:
  - Fever without chills
  - Rarely hypotension
  - In severe cases chills

- Treatment & Prevention
  - Stop transfusion
  - Antipyretics – acetaminophen
  - In case of severe shaking chills - meperidine

- Prevention
  - Leukoreduced blood components

Allergic (Urticarial) Transfusion Reactions

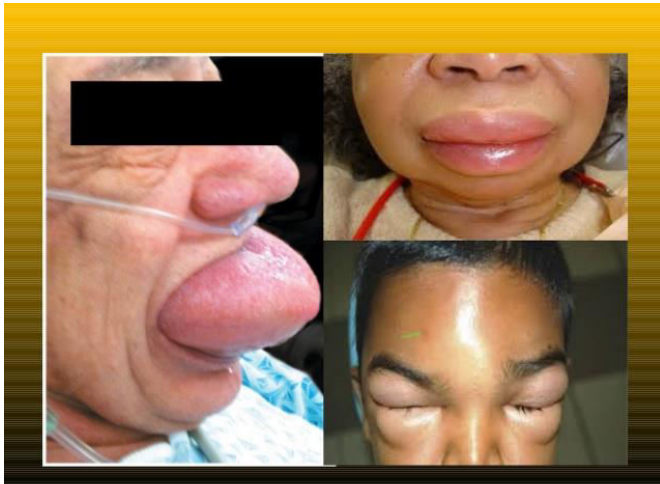
- Common reaction
- Foreign protein in donor plasma react with IgE in the patient
- Donor plasma IgE combine with allergen in patient
- Stimulates mast cells and basophils
- Signs & Symptoms
  - Local erythema, pruritis, hives, fever may or may not
  - Rarely severe – angioneurotic edem, laryngeal edema & bronchial asthma

- Treatment
  - Stop transfusion
  - Antihistaminics – diphenhydramine, Avil
  - Severe cases – corticosteroids
  - Mild reaction – restart transfusion of blood / blood component and observe carefully.

- Prevention
  - Prophylactic administration of antihistaminics one hour before transfusion
  - Repeated reaction – plasma removal by cell washing

Anaphylactic reactions

- Immediate hypersensitivity of immune system
- Range from mild urticaria to severe shock & death
- Fever absent and starts immediately after transfusion few ml of plasma
- Congenitally IgA deficient patient having IgA antibodies
- Signs & Symptoms
  - Respiratory tract – cough, bronchospasm, dyspnea
  - GI tract – nausea, vomiting, diarrhoea
  - Circulatory system – arrhythmias, hypotension,
  - syncope
  - Skin – generalized flushing, urticaria



- Treatment
  - Stop transfusion
  - Maintain i.v. line with NS
  - Inj.Epinephrine SC/IM (Usually about 0.5ml of 1:1000 solution immediately)
  - Maintenance of airway
  - Severe reactions – corticosteroids, aminophylline

- Prevention
  - For RBCs – washing
  - For plasma – plasma for IgA deficient donors

Transfusion related acute lung injury (TRALI)

- Non cardiogenic pulmonary edema or pulmonary hypersensitivity reaction or allergic pulmonary edema

- Leukocyte antibodies in donor or patient plasma

Leukocyte antibodies

Reaction with leukocytes

Activation of complement system

Activation of basophils and platelets

Histamine and serotonin release

Leukocyte emboli aggregating lung capillaries

Interstitial edema and fluid in alveolar air space

- Signs & Symptoms
  - Chills, cough, cyanosis, fever cyanosis, hypotension, increasing respiratory distress
  - X-ray show bilateral pulmonary infilterates

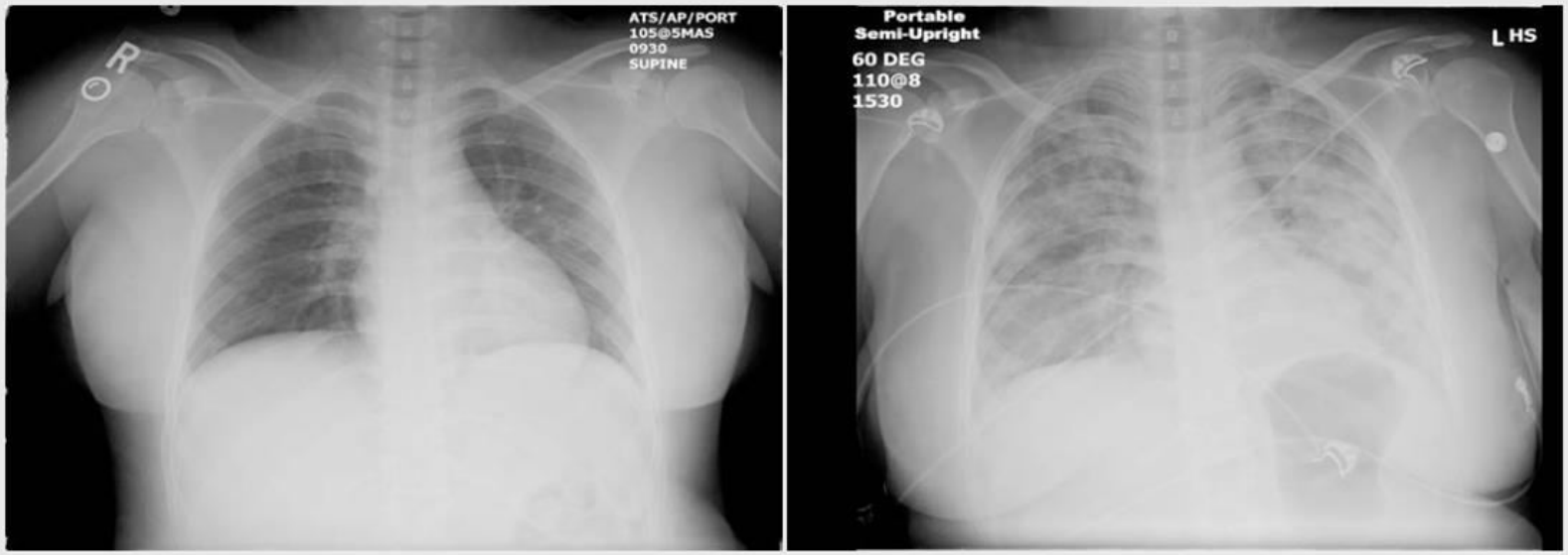


Fig 1: Pre and Post transfusion X-rays of our patient with TRALI. Bilateral Lung infiltrate with pulmonary edema is an essential criteria for the clinical diagnosis of TRALI.

I. TRALI criteria
  A. ALI
    1. Acute onset
    2. Hypoxemia
      a. Research setting:
        1) $PaO_2/FiO_2 \leq 300$, or
        2) $SpO_2 < 90\%$ on room air
      b. Nonresearch setting:
        1) $PaO_2/FiO_2 \leq 300$, or
        2) $SpO_2 < 90\%$ on room air, or
        3) other clinical evidence of hypoxemia
    3. Bilateral infiltrates on frontal chest radiograph
    4. No evidence of left atrial hypertension (ie, circulatory overload)
  B. No preexisting ALI before transfusion
  C. During or within 6 hours of transfusion
  D. No temporal relationship to an alternative risk factor for ALI
II. Possible TRALI
  A. ALI
  B. No preexisting ALI before transfusion
  C. During or within 6 hours of transfusion
  D. A clear temporal relationship to an alternative risk factor for ALI

- Diagnosis of exclusion – heart failure, cardiac overload, bacterial sepsis

- Treatment
  - Supportive care – air way maintenance (O_2 Maintenance)
  - I.V steroids – but effectiveness???
  - Usually pulmonary sufficiency returns with in 10-12 hours

- Prevention
  - Leukocyte poor components

Transfusion associated circulatory overload (TACO)

- Iatrogenic transfusion reaction

- Risk group – young children, elderly patients and patients with chronic normovolemic anemia, cardiac disease etc.

Transfusion at faster rate

Hypervolemia due to transfusion

Congestive heart failure

Pulmonary edema

- Signs & Symptoms
  - Dyspnea, coughing, cyanosis, tachycardia, hypertension, CHF
  - Increased central venous pressure

- Treatment
  - Reduction of hypervolemia – i.v.diuretics
  - Respiratory support – O_2 therapy
  - Cardiac support
  - Therapeutic phlebotomy

- Prevention
  - Plasma reduction
  - Slower rate of transfusion

Table 53-1. Features in TRALI and TACO

Feature	TRALI	TACO
Body temperature	Fever can be present	Unchanged
Blood pressure	Hypotension	Hypertension
Respiratory symptoms	Acute dyspnea	Acute dyspnea
Neck veins	Unchanged	Can be distended
Auscultation	Rales	Rales, S3 may be present
Chest radiograph	Diffuse, bilateral infiltrates	Diffuse, bilateral infiltrates
Ejection fraction	Normal, decreased	Decreased
PA occlusion pressure	18 mmHg or less	Greater than 18 mmHg
Pulmonary edema fluid	Exudate	Transudate
Fluid balance	Positive, even, negative	Positive
Response to diuretic	Minimal	Significant
White count	Transient leukopenia	Unchanged
BNP	<200 pg/mL	>1200 pg/mL
Leukocyte antibodies	Donor leukocyte antibodies present, crossmatch incompatibility between donor and recipient	Donor leukocyte antibodies may or may not be present, positive results can suggest TRALI even with true TACO cases

Bacterial contamination reactions

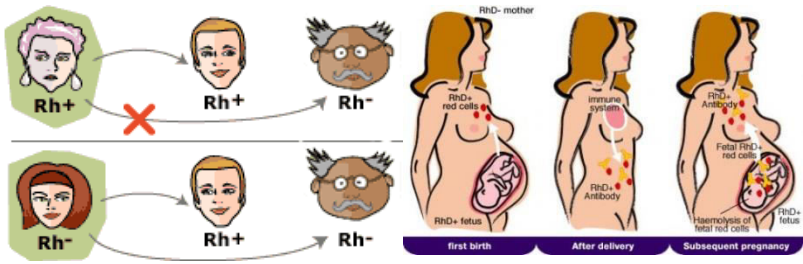
- Rare but can have rapid onset and death. Starts immediately or with in 30 minutes of transfusion
- Endotoxins released during storage
- Most common with platelet transfusions (storage at room temperature)
- Yersinia enterocolitica, pseudomonas species, E.coli (psychrophilic)
- Signs & Symptoms
  - Dryness and flushing of skin, fever, hypotension, chills, muscle pain, vomiting, diarrhea, hemoglobinuria, shock, renal failure and DIC.

- Treatment
  - Stop transfusion immediately
  - Maintain i.v.line
  - Broad spectrum antibiotics
  - Therapy for shock, steroids, vasopressor
  - Fluid support, respiratory ventilation
  - Maintenance of renal function

- Prevention
  - Strict adherence to all procedures (blood collection)

Delayed Hemolytic Transfusion Reaction (DHTR)

- Primary alloimmunization
  - Occurs several weeks after transfusion and mostly mild
  - Due to incompatibility of Rh, Kell, Duffy, Kidd and other systems
- Secondary or anamnestic response
  - Transfusion of incompatible RBCs in a patient who is already immunized
- Signs & Symptoms
  - Mild fever
  - Fall in hemoglobin
  - Rise in bilirubin 5-7 days after transfusion
  - Renal failure very rare
- Treatment
  - Transfusion with compatible blood (in chronic transfused patients)



Post transfusion purpura (PTP)

- Rapid onset thrombocytopenia as a result of anamnestic production platelet alloantibody
- Usually occurs in multiparous female and 7-14 days after transfusion
- Antibody specificity – HPA-1a (anti-$P1^{A1}$)

- Signs and symptoms
  - Fever, chills, dyspnea
  - Severe cases – generalized purpura, hematuria, malena and vaginal bleeding
- Treatment
  - Corticosteroids
  - Plasma exchange (Plasmapheresis)
  - Intravenous immunoglobulin)

Transfusion associated graft Vs host disease (TAGVHD)

- Phenomenon that can occur after blood transfusion in which donor T cells, responding to proteins on host cells, proliferate and target host organs, primarily the skin, liver, intestinal tract, and marrow.

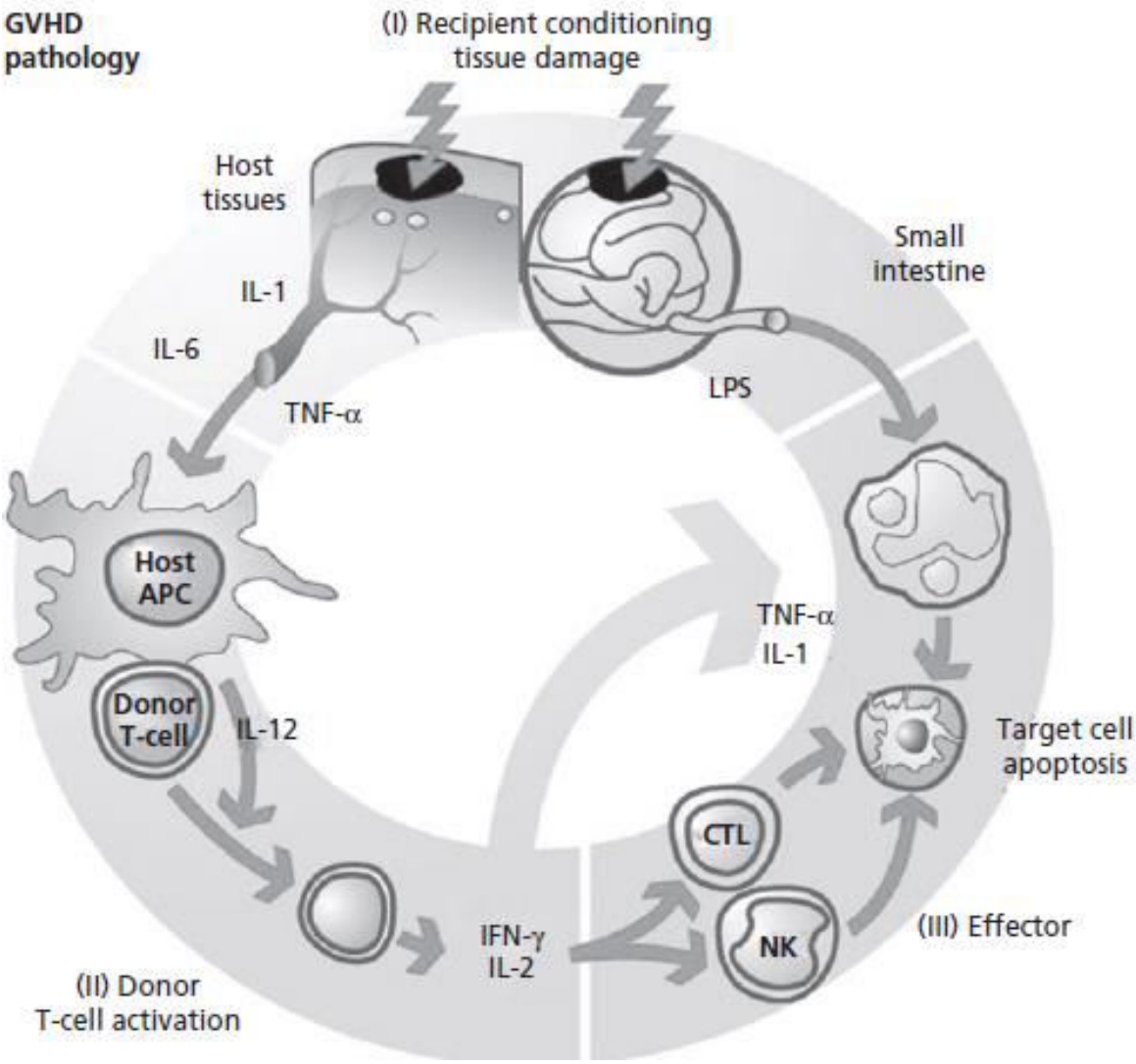
- Risk group
  - Lymphopenic and bone marrow suppressed patients
  - very low birth weight premature infants,
  - Critically ill patients receiving extracorporeal membrane oxygenation
  - Individuals with congenital immune deficiencies
  - Recipients of blood transfusions from family members.

- Requirements to develop GVHD
  - Graft must contain immunologically competent cells
  - There must be antigenic differences between the donor and the recipient
  - The recipient must be unable to mount an effective immunologic response to eradicate the transplanted immunologically competent cells

The presentation of host protein todonor T cells by antigen-presenting cells (APCs)

Donor T-cell activation, proliferation, and migration

Host target tissue damage


GVHD pathology
(I) Recipient conditioning tissue damage
Host tissues
IL-1
IL-6
TNF-α
LPS
Small intestine
Host APC
Donor T-cell
IL-12
TNF-α
IL-1
Target cell apoptosis
CTL
NK
IFN-γ
IL-2
(II) Donor T-cell activation
(III) Effector

- Signs & Symptoms
  - Fever
  - Skin rashes
  - Hepatitis
  - Diarrhea
  - Bone marrow suppression
  - Infection

- Treatment
  - High steroids
  - Cyclosporine, methotrexate, azathioprine
  - Antithymocyte globulin

- Prevention
  - Irradiation of blood and blood components

Table 54-2. Comparison of GVHD Following Hematopoietic Stem Cell Transplantation with Transfusion-Associated GVHD*

Manifestation	HSCT GVHD	TA-GVHD
Median onset (range)	23 days (12-100 days)	10 days (2-30 days)
Fever	Often	Usually
Skin rash	+	+
Liver involvement	+/−	+
Gastrointestinal involvement	+/−	+/−
Pancytopenia	Rare	Almost always
Occurrence	25%-50%	Rare
Response to therapy	35%-50%	Rare
Mortality	10%-25%	90%-100%

*Modified from Brubaker.[113]

Iron overload

- Transfusion induced hemosiderosis
- Each unit of red cell contain 225 mg of iron
- Occurs in chronic transfusion dependent patients
  - Congenital hemolytic anemias
  - Aplastic anemia
  - Chronic renal failure
- Iron mainly affect (interfere with mitochondrial function) – heart, liver and endocrine glands

- Signs & Symptoms
  - Muscle weakness, fatigue, weight loss
  - Mild jaundice, anemia
  - Mild diabetes
  - Cardiac arrhythmias

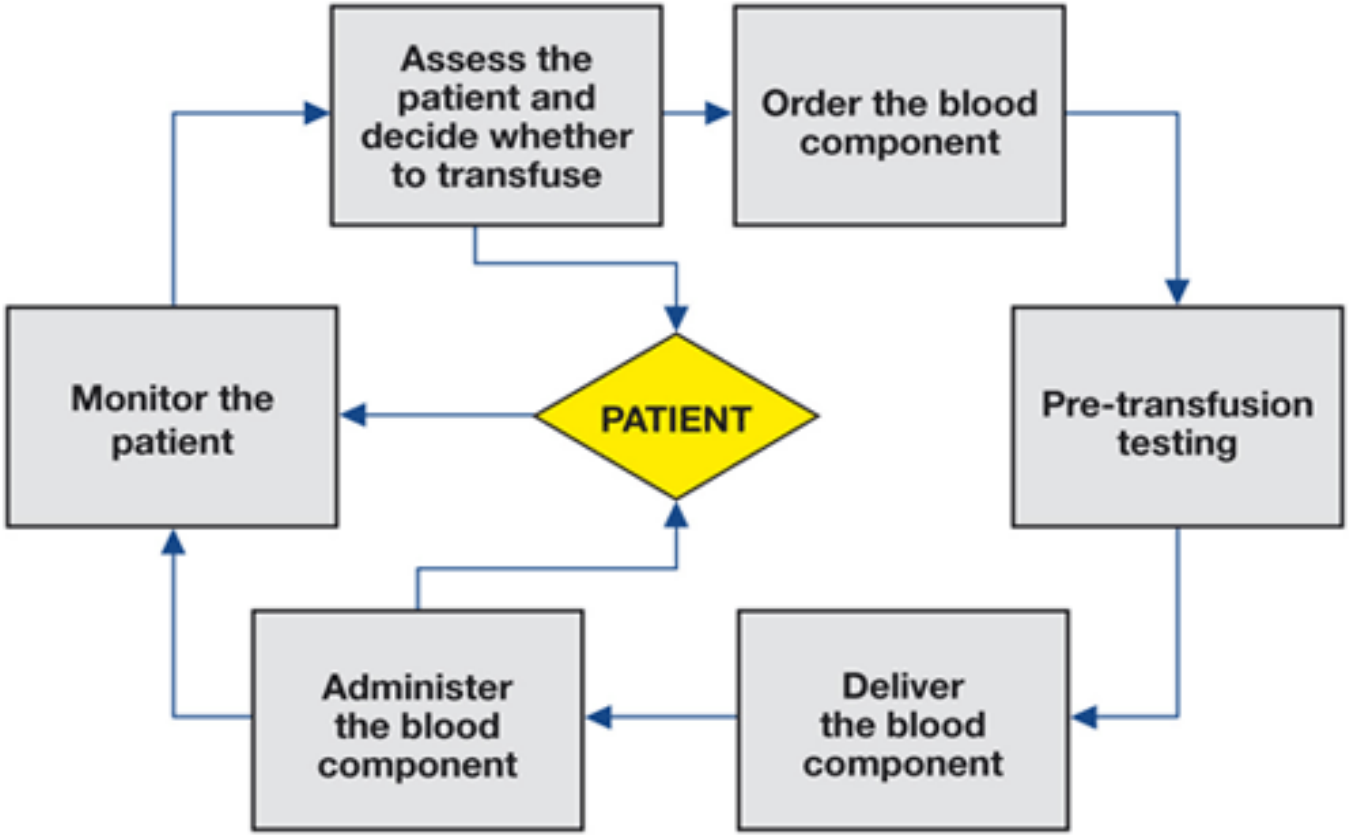
- Treatment
  - Iron chelating agents – Subcutaneous or oral
  - Therapeutic phlebotomy

- Prevention
  - One promising strategy – neocyte (young Red cells) transfusion to reduce frequency of transfusion

Transfusion Transmitted Infections

- Testing of donated blood for HIV, Hepatitis B, Hepatitis C, Malaria, Syphilis is mandatory.
- HIV – 5 days (by NAT)
- Hepatitis B – 25 days (by NAT)
- Hepatitis C – 5 days (by NAT)

Transfusion Reactions



Investigation of transfusion reaction

- Necessary for
  - Diagnosis
  - Selection of appropriate therapy
  - Transfusion management
  - Prevention of future transfusion reactions

- Any investigation should include following data
  - Diagnosis
  - Medical history of pregnancies, transplants and previous transfusions
  - Current medication
  - Clinical signs and symptoms of reaction

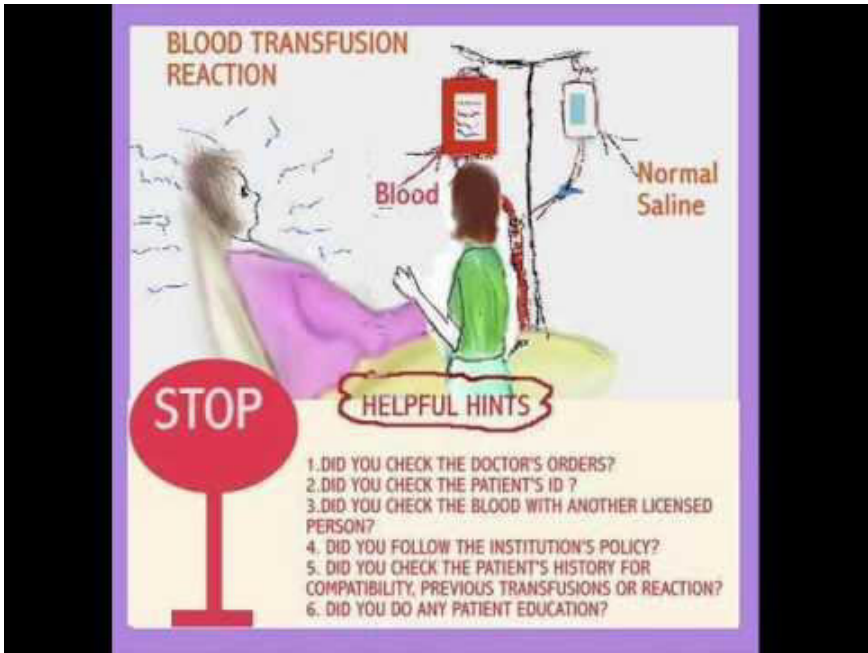
- Any transfusion history should include
  - How much volume transfused
  - How fast
  - RBCs were cold or warm and given under any pressure?
  - Any drugs at the time of transfusion

Table 53-3. Overlapping Signs and Symptoms of Transfusion Reactions

Sign or Symptom	Possible Reaction	Most Likely > Less Likely Blood Component*
Fever, chills	Febrile nonhemolytic Septic Acute hemolytic TRALI	Platelets (especially septic) >RBCs >Plasma
Urticaria, pruritus	Allergic Anaphylactic	Plasma >Platelets >RBCs
Dyspnea	TACO TRALI Anaphylactic	Any
Hypotension	Septic Hypotensive Acute hemolytic Anaphylactic	Platelets >plasma >RBCs

Investigations

- Immediate
  - Clerical checks
  - Visual inspection of patient plasma and blood bag
- Required
  - ABO & Rh grouping of patient (pre and post transfusion) and blood bag
  - Cross matching of patient (pre and post transfusion) sample with donor bag
  - DCT & ICT
  - Antibody screening
  - Free hemoglobin in patient sample
  - Bilirubin – unconjugated and total
  - Urine routeine
- Extended
  - Blood bag for culture
  - Grams staining
  - Serum haptoglobin



NARAYANA MEDICAL COLLEGE & HOSPITAL

CHINTHAREDDYPALEM, NELLORE

DEPARTMENT OF TRANSFUSION MEDICINE AND BLOOD BANK

LICENCE NO. - 08/NL/AP/2007/BB/G

COMPATIBILITY REPORT

Patient Details: **Date:**

Name: Age/Sex: Blood Group:

Hospital: Reg./I.P.No: Ref. Doctor:

Diagnosis: Ward: Bed No:

Bag Details:

Bag No.: Screening for T I Is: Blood Group:

WB / Component: Volume:

Compatibility Details:

Date & Time of Crossmatch: Result of Crossmatch:

Date & Time of Issue:

Performed by **Checked by** **Signature of Medical Officer**

NARAYANA MEDICAL COLLEGE & HOSPITAL

CHINTHAREDDYPALEM, NELLORE

DEPARTMENT OF TRANSFUSION MEDICINE AND BLOOD BANK

LICENCE NO. - 08/NL/AP/2007/BB/G

TRANSFUSION FEEDBACK FORM

Patient Details: **Date:**

Name: Age/Sex: Blood Group:

Hospital: Reg./I.P.No: Ref. Doctor:

Diagnosis: Ward: Bed No:

Bag Details:

Bag No.: Blood Group: WB / Component:

Volume:

Transfusion Details: (mention date and time)

Bag reached at: Started at: Completed at:

Rate of Transfusion:

Reason for delay in transfusion if any:

Vitals	Pre Transfusion	During Transfusion	Post Transfusion
Pulse			
B.P			
Temperature			
Respiratory Rate			

Note: In case of Transfusion reaction, kindly fill up the transfusion reaction form and inform blood bank staff immediately and send suitable samples to blood bank for worku

Signature of Nursing Staff **Signature of Doctor**

NARAYANA MEDICAL COLLEGE HOSPITAL
DEPARTMENT OF TRANSFUSION MEDICINE
TRANSFUSION ADVERSE REACTION REPORTING FORM

Instructions:
1. Please send 3ml of EDTA & Plain Post transfusion patient blood sample
2. First voided urine sample after transfusion reaction
3. Send blood bag along with transfusion set

Patient Identification

Name: Age/Sex: Registration/I.P.No:

Ward: Diagnosis: Refered Doctor:

Transfusion History: Yes/No If Yes, any reaction:

Tansfusion Information

Transfused Blood product:

Whole blood ☐ Packed red cells ☐ FFP ☐ Platelets ☐ Cryoprecipitate ☐

Bag details:

Bag No: Blood group: Date of collection: Date of expiry: Volume:

Transfusion Date:

Time of the transfusion started:

Time when adverse reaction detected:

Volume transfused to patient till the time of reaction:

Pre-transfusion Bilirubin: Total: Direct: Indirect:

Symptoms

Minor Transfusion reaction		Suggested major transfusion reaction	
☐ Fever ……(>1°C above baseline)		☐ Backache	☐ Chest Pain
☐ Chills	☐ Rash	☐ Pain at infusion site	☐ Tachycardia
☐ Itching	☐ Nausea	☐ Hypotension	☐ Hypertension
☐ Flushing		☐ Dyspnea	☐ Oliguria
☐ Others……		☐ Jaundice	☐ Haematuria
		☐ Bleeding tendency	☐ Others……..

Vital signs & Management:

	Pre–Transfusion	Post–Transfusion
Temperature		
Blood Pressure		
Pulse		
Management		
Outcome ☐ Complete recovery ☐ Recovered with complication ☐ Death		

Reported by Dr. _____ Date:_____

Signature _____

NARAYANA MEDICAL COLLEGE HOSPITAL
DEPARTMENT OF TRANSFUSION MEDICINE
TRANSFUSION ADVERSE REACTION WORKUP FORM

Patient Identification

Name: Age/Sex:

Registration/I.P.No: Ward:

Diagnosis: Refered Doctor:

Transfusion History: Yes/No If Yes, any reaction:

Tansfusion Information

Transfused Blood product:

Whole blood ☐ Packed red cells ☐ FFP ☐ Platelets ☐ Cryoprecipitate ☐

Bag details: Bag No :

Blood Group : Appearance : Date of collection:

Rh type : Volume : Date of Expiry :

Transfusion Date:

Time of the transfusion started:

Time when adverse reaction detected:

Volume transfused to patient till the time of reaction:

Clerical Error:…….

Compatability testing

Grouping & Rh typing:

Bag Blood Group :

Pretransfusion Sample : Post transfusion Sample:

Cross – matching details:

Sample	Saline	Coombs
Pre transfusion		
Post transfusion		

Auto – control : Direct Coombs Test :

Indirect Coombs Test : Antibody Screening :

Serum bilirubin :Pre transfusion: Post Transfusion :

Sterility of the blood bag:

Inference……..

Signature of Medical Officer

Take Home Message

- Stop TX immediately and keep an IV open with 0.9 %Saline
- Contact the clinician
- Check vital signs every 15 minutes
- Check labels, forms and Ids
- Send blood bag along with transfusion set &patient's plain and EDTA sample to BB for further workup
- Send patient sample for investigations like LFT, RFT, Routine Urine Examination & Peripheral Smear.


THANK
YOU!


DONATE
BLOOD