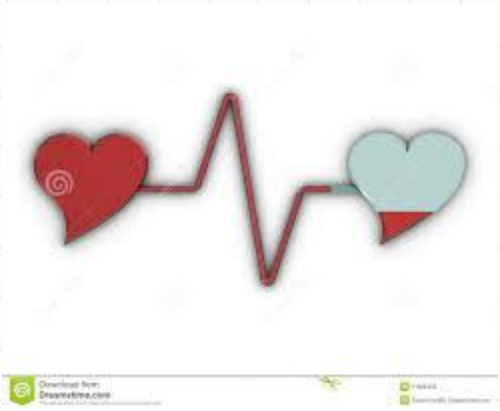

Transfusion Medicine and Therapy

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Objective

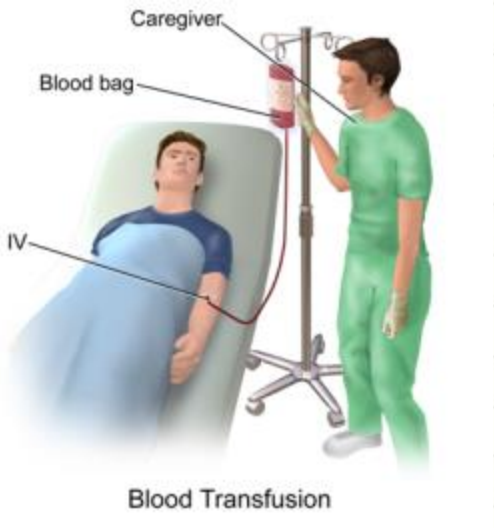
- Indication of blood transfusion
- Blood groups
- Blood component
- Blood transfusion complication treatment
- Alternatives to Blood Products

PERSPECTIVE

- The era of modern blood transfusion began in the early 1900s with discovery of the ABO red cell antigen system.

- World War I it was known that adding citrate enabled the storage of anticoagulated blood.

Blood Banking



Blood Transfusion

Blood Collection

- Blood centers, process more than 90% of the units collected .
- Traditional allogenic donation methods still predominate, but increasing use is being made of red cell apheresis technology, by which red cells are separated from the blood at the time of collection, with the rest returned to circulation.

Anticoagulants in Blood

- Blood collection bags contain an anticoagulant-preservative of citrate, phosphate, dextrose, and adenine (CPDA-1)
- Ensuring a shelf life (viability of at least 70% of the RBCs 24 hours after infusion) of 35 days and hematocrit of 70 to 80% for PRBCs.
- Additive solutions (Adsol, Nutricel, Optisol) provide additional nutrients, extending maximum storage to 42 days and lowering viscosity, which makes infusion easier.

Storage of Blood

- Storage impairs red cell function. Transfused blood delivers oxygen to the tissues less efficiently.
- Refrigerated at 1 to 6° C (usually 4° C), cell metabolism continues and changes occur .
- < in pH and in the level of 2,3-DPG.
- The deformability of RBCs makes them, over time, more spherical and rigid, thereby increasing resistance to capillary flow.
- Cell leakage of potassium(≈ 6 mEq/U).

Blood Typing

- Identified red blood cell (RBC) :
- ABO and related carbohydrate antigens (H, P, I, and Lewis), the 48 Rh system antigens, and more than 200 non-ABO/Rh antigens.
- Blood specimen from the patient is sent for the following tests: ABO grouping, Rh typing, and an antibody screen for unexpected (non-ABO/Rh) antibodies.

ABO Grouping

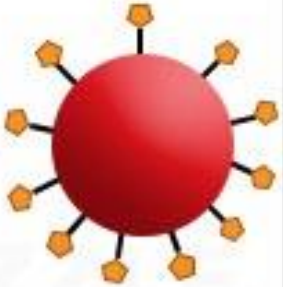
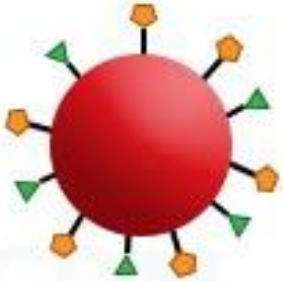
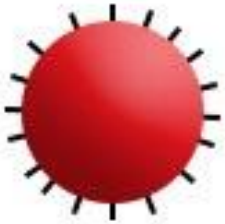
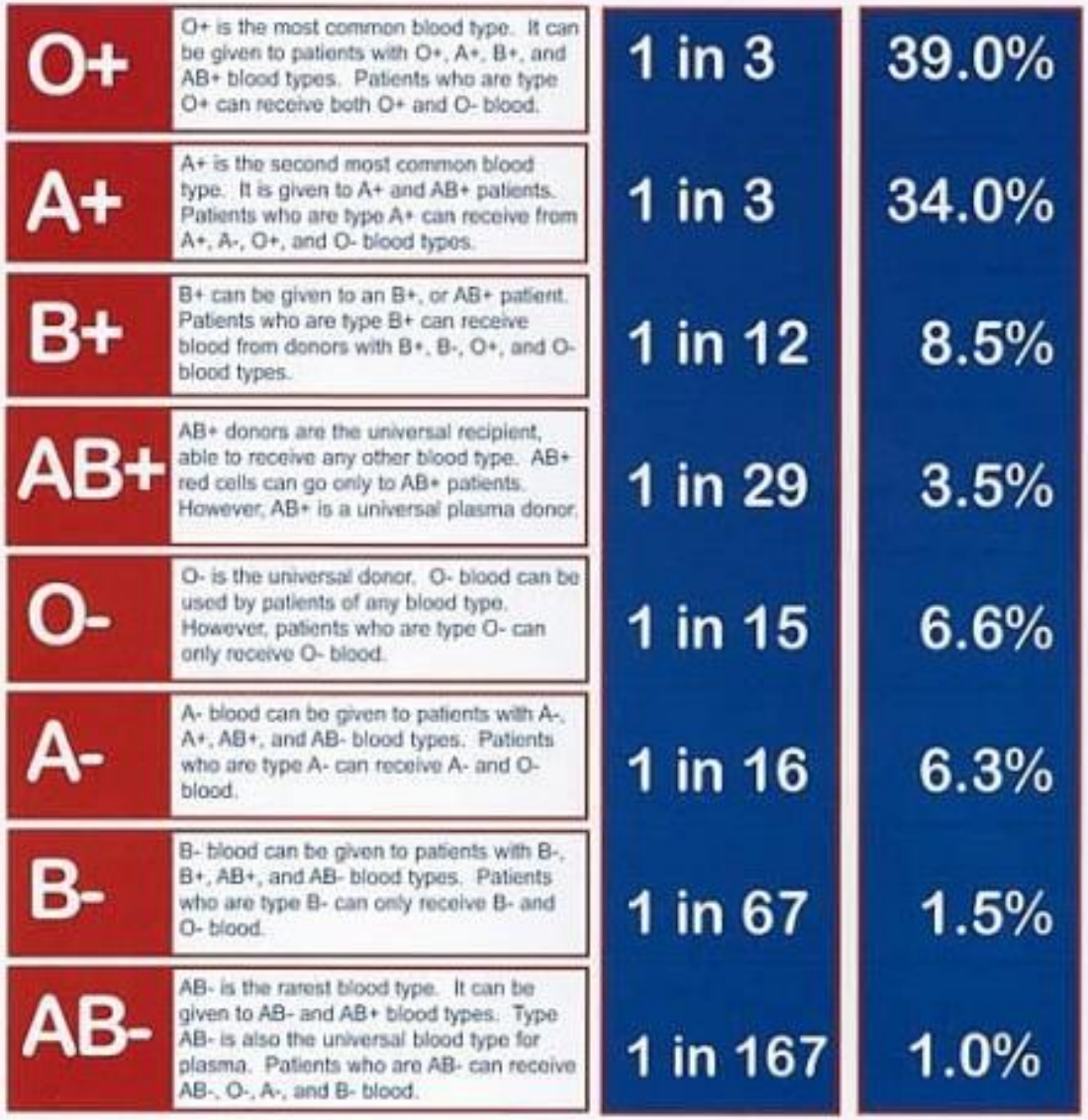
	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-B and Anti-A
Antigens in Red Blood Cell	 A antigen	 B antigen	 A and B antigens	None

TABLE 113-1 RBC Blood Group Systems and Alloantigens

Blood Group System	Antigen	Alloantibody	Clinical Significance
Rh (D, C/c, E/e)	RBC protein	IgG	HTR, HDN
Lewis (Le^a, Le^b)	Oligosaccharide	IgM/IgG	Rare HTR
Kell (K/k)	RBC protein	IgG	HTR, HDN
Duffy (Fy^a/Fy^b)	RBC protein	IgG	HTR, HDN
Kidd (Jk^a/Jk^b)	RBC protein	IgG	HTR (often delayed), HDN (mild)
I/i	Carbohydrate	IgM	None
MNSsU	RBC protein	IgM/IgG	Anti-M rare HDN, anti-S, -s, and -U HDN, HTR

Abbreviations: RBC, red blood cell; HDN, hemolytic disease of the newborn; HTR, hemolytic transfusion reaction.


O+
O+ is the most common blood type. It can be given to patients with O+, A+, B+, and AB+ blood types. Patients who are type O+ can receive both O+ and O- blood.
1 in 3
39.0%
A+
A+ is the second most common blood type. It is given to A+ and AB+ patients. Patients who are type A+ can receive from A+, A-, O+, and O- blood types.
1 in 3
34.0%
B+
B+ can be given to an B+, or AB+ patient. Patients who are type B+ can receive blood from donors with B+, B-, O+, and O- blood types.
1 in 12
8.5%
AB+
AB+ donors are the universal recipient, able to receive any other blood type. AB+ red cells can go only to AB+ patients. However, AB+ is a universal plasma donor.
1 in 29
3.5%
O-
O- is the universal donor. O- blood can be used by patients of any blood type. However, patients who are type O- can only receive O- blood.
1 in 15
6.6%
A-
A- blood can be given to patients with A-, A+, AB+, and AB- blood types. Patients who are type A- can receive A- and O- blood.
1 in 16
6.3%
B-
B- blood can be given to patients with B-, B+, AB+, and AB- blood types. Patients who are type B- can only receive B- and O- blood.
1 in 67
1.5%
AB-
AB- is the rarest blood type. It can be given to AB- and AB+ blood types. Type AB- is also the universal blood type for plasma. Patients who are AB- can receive AB-, O-, A-, and B- blood.
1 in 167
1.0%

Blood Typing

- The “forward type” determines the ABO and Rh phenotype of the recipient’s RBC by using antiserum directed against the A, B, and D antigens.
- The “reverse type” detects isoagglutinins in the patient’s serum and should correlate with the ABO phenotype, or forward type.

Blood Typing

- ABO grouping requires that the recipient's red cells be tested with anti-A and anti-B serum, and that their serum be tested with A and B red cells.
- Those with type AB blood form no ABO group antibodies.(universal recipient).
- Those with type O have antibodies against both.(universal donor).
- Rh typing can usually be determined by adding a commercial reagent (anti-D) to recipient RBCs.

Recipient's blood			Reactions with donor's red blood cells			
ABO antigens	ABO antibodies	ABO blood type	Donor type O cells	Donor type A cells	Donor type B cells	Donor type AB cells
None	Anti-A Anti-B	O				
A	Anti-B	A				
B	Anti-A	B				
A & B	None	AB				

Compatible

Not compatible

Type and Screen

- The type and screen allows quicker selection of appropriate banked blood for complete crossmatch if a transfusion is ordered.
- When a blood transfusion is ordered, a formal crossmatch is done by mixing recipient serum with donor RBCs as a final compatibility test prior to transfusion.

Cross Match

- This can be done using a Coombs test (with serum incubated to 37° C), or the more rapid “immediate spin crossmatch” at room temperature, which will detect only ABO incompatibility.
- Thorough Coombs test can detect incompatibilities that were missed with the antibody screen.

Blood and Products Transfusion

Why?

- Increase oxygen carrying capacity
- Restoration of red cell mass
- Correction of bleeding caused by platelet dysfunction
- Correction of bleeding caused by factor deficiencies

Oxygen Delivery

- Oxygen Delivery (DO_2) is the oxygen that is delivered to the tissues

  DO_2= COP x CaO_2
- Cardiac Output (CO) = HR x SV
- Oxygen Content (CaO_2):
  - (**Hgb** x 1.39)O_2 saturation + PaO_2(0.003)
  - Hgb is the main determinant of oxygen content in the blood

Oxygen Delivery (cont.)

- Therefore: **DO_2 = HR x SV x CaO_2**

- If HR or SV are unable to compensate, Hgb is the major determinant factor in O_2 delivery

Administration

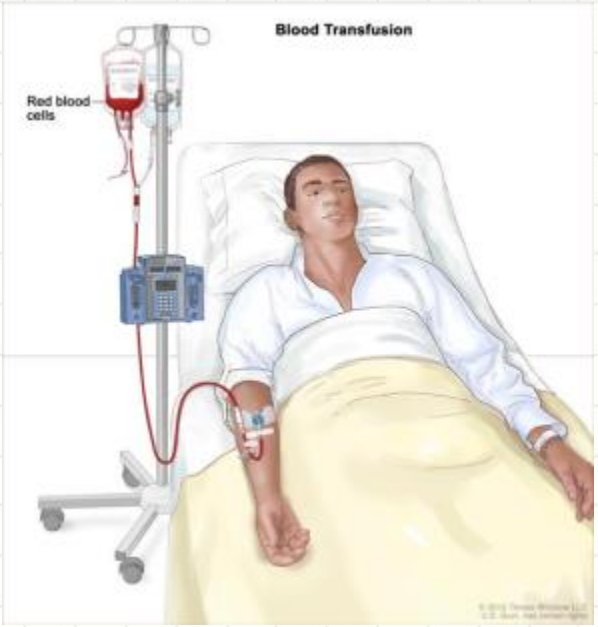
- Legal Aspects:
- Two qualified personnel check it at the bedside to prevent a potentially fatal clerical error.
- Recipient and unit identification, confirmation of compatibility, expiration date.
- 60% of transfusions occur perioperatively.
- responsibility of transfusing perioperatively is with the anesthesiologist

Administration

- Urgent transfusion situations require flow rates faster than gravity can provide.
- Pressure bags are available that completely encase the blood bag and apply pressure evenly to the blood bag surface.
- If external pressure is anticipated, large-bore needles are recommended for venous access to prevent hemolysis.

Administration

- If only a small-gauge needle is available, the transfusion may be diluted with normal saline, but this may cause unwanted volume expansion.



MANAGEMENT

1. Patient's age,
2. severity of symptoms,
3. cause of the deficit,
4. underlying medical condition,
5. ability to compensate for decreased oxygen-carrying capacity, and
6. tissue oxygen requirements are all considered.

Management

Clinical evaluation:

1. appearance (pallor, diaphoresis),
2. mentation (alert, confused),
3. heart rate,
4. blood pressure,
5. nature of the bleeding (active, controlled, uncontrolled),

Laboratory evaluation :

1. Hgb,
2. hematocrit,
3. platelets,
4. clotting functions.

When to Transfuse?

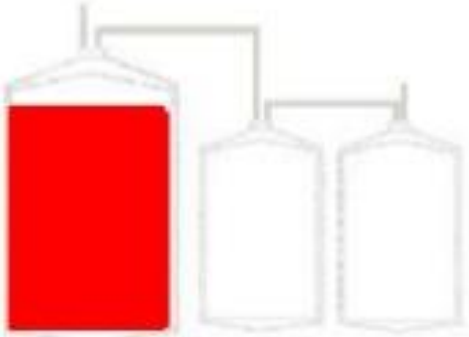
- TRICC (Transfusion Requirements in Critical Care) trial, demonstrated that in the critical care setting, a transfusion threshold of 7 g/dL was as safe as a threshold of 10 g/dL.

- A subgroup analysis generated some concern that patients with ischemic heart disease benefit from higher transfusion threshold

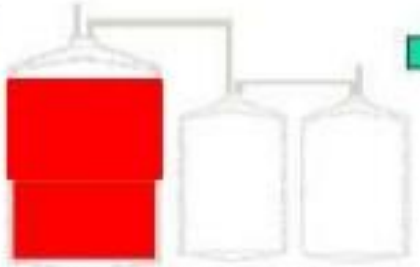
Blood Products

- Whole Blood
  - Packed RBCs
  - Platelet-rich Plasma
    - Plasma
      - Cryoppt-reduced Plasma
      - Cryoprecipitate
      - Plasma Derivatives
        - Albumin
        - IVIg
    - Platelets

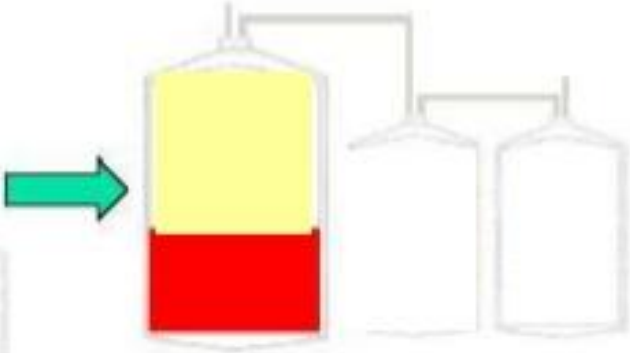
Blood Component Preparation



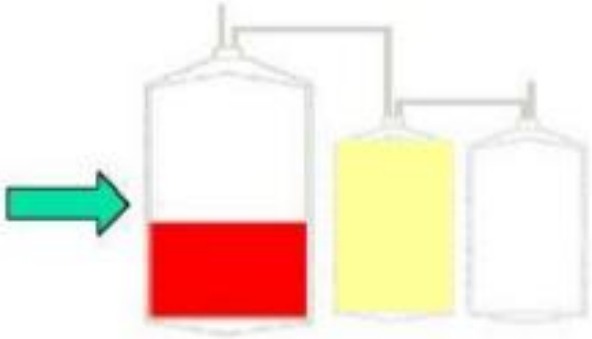
Blood is collected as whole blood



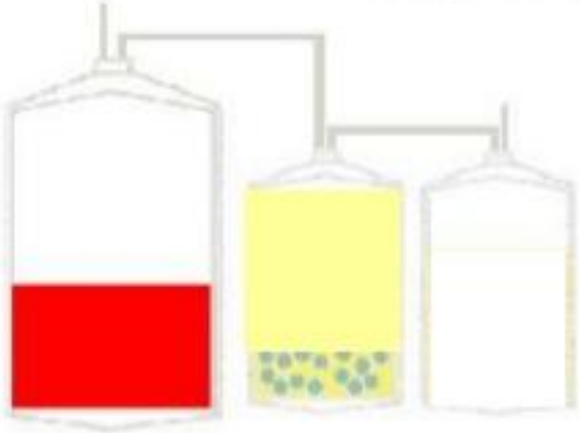
This is done by light centrifugation



The platelet rich plasma can then be expressed off, leaving packed red blood cells



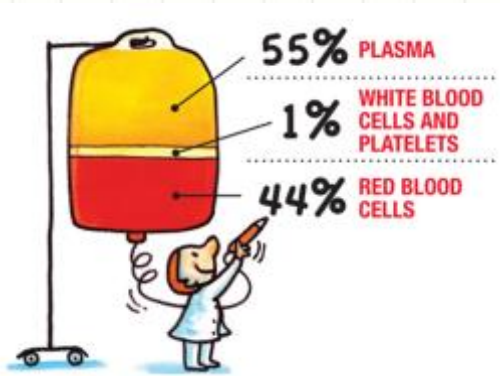
The plasma can be centrifuged heavily a second time to separate the platelet rich plasma.



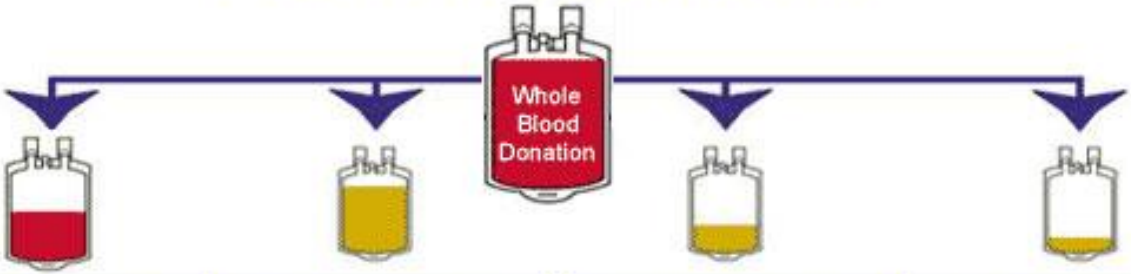
The supernatant plasma can be expressed into a third bag and stored as fresh frozen plasma (FFP). The remaining platelet rich plasma is utilized as a platelet pack.

Blood and its components

- **Whole Blood** is not as economical as component therapy, although there has recently been renewed interest in the benefits of using fresh whole blood in military field hospitals.
- In modern transfusion medicine is rarely used.



The potential of HUMAN BLOOD



Red Blood Cells	Fresh Frozen Plasma	Concentrate of Platelets	Cryoprecipitate
To increase the amount of red blood cells after trauma or surgery or to treat severe anemia.	To correct a deficiency in coagulation factors or to treat shock due to plasma loss from burns or massive bleeding.	To treat or prevent bleeding due to lowplatelet levels. To correct functional platenet problems	To treat fibrinogen deficiencies:
STORAGE PERIOD			
42 days in the refrigerator or 10 years in the freezer	1 year in the freezer	5 days at room temperature	1 year in the freezer

Blood and its components

Packed Red Blood Cells

- PRBCs are given to improve oxygen delivery to tissues at the microvascular level.
- American Society of Anesthesiologists :

1. Transfusion is rarely needed with a Hgb concentration greater than 10 g/dL .
2. Always needed when the Hgb is less than 6 g/dL.
3. Patients with a Hgb between 6 and 10 mg/dL require careful clinical judgment.

Blood and its components

- PRBCS …
- Ischemic heart disease may render patients more intolerant of anemia, although more research is needed to clarify whether transfusion benefits these patients.

- Physicians would still transfuse a patient with ongoing hemorrhage and unstable vital signs despite adequate fluid resuscitation, and would occasionally consider withholding transfusion for Hgb levels even lower than 6 g/dL in a young, healthy, asymptomatic patient without ongoing hemorrhage.

Blood and its components

PRBCS

- In an average adult, 1 U of PRBCs increases the Hgb by about 1 g/dL or the hematocrit by about 3%.
- PRBCs are run through a filter with a large-bore intravenous line with normal saline.
- Lactated Ringer's solution can lead to clotting due to the added calcium, and hemolysis may result with a hypotonic solution.
- Most transfusions are given over 60 to 90 minutes (not longer than 4 hours).
- Unused blood should be returned promptly to the blood bank because any units unrefrigerated for more than 30 minutes are discarded

Blood and its components

Fresh Frozen Plasma

- A unit of FFP typically has a volume of 200 to 250 mL, is ABO compatible, and is given through blood tubing within 2 to 6 hours of thawing.
- It contains all clotting factors.

- It should be given in doses calculated to achieve a minimum of 30% of plasma factor concentration, traditionally calculated as 10 to 15 mL/kg of FFP.

Blood and its components

Blood and its components

Platelets

- Cross-matching is unnecessary, but Rh-negative patients should receive Rh-negative platelets .(may cause Rh sensitization).
- In adults the traditional dose has been 4 to 6 U (a “six pack”of platelets).
- In children it is 1 U/10 kg body weight.

Blood and its components

Blood and its components

CRYOPRECIPITATE

Cryoprecipitate is a source of fibrinogen, factor VIII, and von

Willebrand factor (vWF). It is ideal for supplying fibrinogen tothe volume-sensitive patient.

When factor VIII concentrates are not available, cryoprecipitate may be used since each unit contains approximately 80 units of factor VIII.

Cryoprecipitate may also supply vWF to patients with dysfunctional (type II) or absent (type III) von Willebrand disease.

Blood and its components

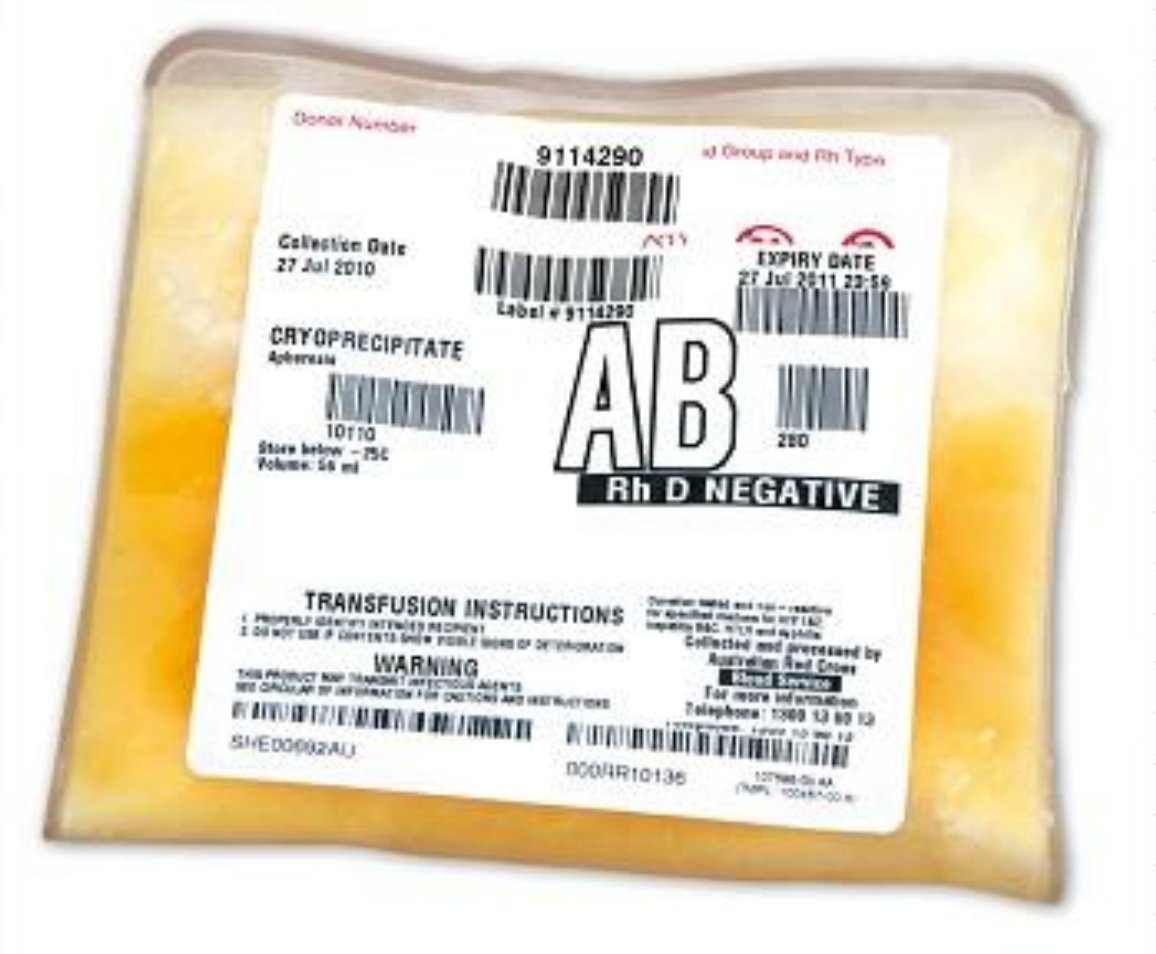


TABLE 113-2 Characteristics of Selected Blood Components

Component	Volume, mL	Content	Clinical Response
PRBC	180–200	RBCs with variable leukocyte content and small amount of plasma	Increase hemoglobin 10 g/L and hematocrit 3%
Platelets	50–70	5.5×10^{10}/RD unit	Increase platelet count 5000–10,000/μL
	200–400	$\geq 3 \times 10^{11}$/SDAP product	CCI $\geq 10 \times 10^{9}$/L within 1 h and $\geq 7.5 \times 10^{9}$/L within 24 h posttransfusion
FFP	200–250	Plasma proteins—coagulation factors, proteins C and S, antithrombin	Increases coagulation factors about 2%
Cryoprecipitate	10–15	Cold-insoluble plasma proteins, fibrinogen, factor VIII, vWF	Topical fibrin glue, also 80 IU factor VIII

Abbreviations: CCI, corrected count increment; FFP, fresh-frozen plasma; PRBC, packed red blood cells; RBC, red blood cell; RD, random donor; SDAP, single-donor apheresis platelets; vWF, von Willebrand factor.

Adverse Reactions of Blood Transfusion

- The most common reactions are not life threatening, although serious reactions can present with mild symptoms and signs.
- Reactions can be reduced or prevented by modified (filtered, washed, or irradiated) blood components.

Adverse Reactions of Blood Transfusion

IMMUNE-MEDIATED REACTIONS

Acute hemolytic transfusion reactions

- Immune-mediated hemolysis occurs when the recipient has preformed antibodies that lyse donor erythrocytes.
- The ABO isoagglutinins are responsible for the majority of these reactions, although alloantibodies directed against other RBC antigens, i.e., Rh, Kell, and Duffy, may result in hemolysis.

Adverse Reactions of Blood Transfusion

- AHTR present with hypotension, tachypnea, tachycardia, fever, chills, hemoglobinemia, hemoglobinuria, chest and/or flank pain, and discomfort at the infusion site.
- Transfusion must be stopped immediately, intravenous access maintained, and the reaction reported to the blood bank.
- The laboratory evaluation for hemolysis :

1. measurement of serum haptoglobin,
2. lactate dehydrogenase (LDH), and
3. indirect bilirubin levels.

Adverse Reactions of Blood Transfusion

- Treatment of AHTR:
- The immune complexes that result in RBC lysis can cause renal dysfunction and failure.
- Diuresis should be induced with intravenous fluids and furosemide or mannitol.
- Tissue factor released from the lysed erythrocytes may initiate DIC.
- Coagulation studies like prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, and platelet count should be monitored in patients with hemolytic reactions.

Adverse Reactions of Blood Transfusion

- Febrile nonhemolytic transfusion reaction
- The most frequent reaction associated with the transfusion of cellular blood components is a febrile nonhemolytic transfusion reaction(FNHTR).
- These reactions are characterized by chills and rigors and a ≥1°C rise in temperature.

Adverse Reactions of Blood Transfusion

Allergic reactions

- Urticarial reactions are related to plasma proteins found in transfused components.
- Mild reactions treated symptomatically by temporarily stopping the transfusion and administering antihistamines (diphenhydramine, 50 mg orally or IM).

Adverse Reactions of Blood Transfusion

Anaphylactic reaction

- This severe reaction presents after transfusion of a few milliliters of the blood component.
- Symptoms and signs: difficulty in breathing, coughing, nausea and vomiting, hypotension, bronchospasm, loss of consciousness, respiratory arrest, and shock.
- Stopping the transfusion, maintaining vascular access, and administering epinephrine (0.5–1 mL of 1:1000 dilution subcutaneously).
- Glucocorticoids may be required in severe cases.

Adverse Reactions of Blood Transfusion

Graft-versus-host disease

- Graft-versus-host disease (GVHD) is a frequent complication of allogeneic stem cell transplantation, in which lymphocytes from the donor attack and cannot be eliminated by an immunodeficient host.
- Mediated by donor T lymphocytes that recognize host HLA antigens as foreign and mount an immune response
- Manifested clinically by fever, a characteristic cutaneous eruption, diarrhea, and liver function abnormalities.

Adverse Reactions of Blood Transfusion

Transfusion-related acute lung injury

- Presents as acute respiratory distress, either during or within 6 h of transfusing the patient.
- Characterised by respiratory compromise and signs of noncardiogenic pulmonary edema, including bilateral interstitial infiltrates on chest x-ray.
- Treatment is supportive, and patients usually recover without sequelae.

Adverse Reactions of Blood Transfusion

NONIMMUNOLOGIC REACTIONS

Fluid overload

- Blood components are excellent volume expanders, and transfusion may quickly lead to volume overload.
- Monitoring the rate and volume of the transfusion and using a diuretic can minimize this problem.

Adverse Reactions of Blood Transfusion

Hypothermia

- Refrigerated (4°C) or frozen (–18°C or below) blood components can result in hypothermia when rapidly infused.
- Cardiac dysrhythmias can result from exposing the sinoatrial node to cold fluid.
- Use of an in-line warmer will prevent this complication.

Adverse Reactions of Blood Transfusion

Electrolyte toxicity

- RBC leakage during storage increases the concentration of potassium in the unit.
- Citrate, commonly used to anticoagulate blood components, chelates calcium and thereby inhibits the coagulation cascade.
- Hypocalcemia, manifested by circumoral numbness and/or tingling sensation of the fingers and toes, may result from multiple rapid transfusions.

- Citrate is quickly metabolized to bicarbonate, calcium infusion is seldom required in this setting.

Adverse Reactions of Blood Transfusion

Iron overload

- Each unit of RBCs contains 200–250 mg of iron. Symptoms and signs of iron overload affecting endocrine, hepatic, and cardiac function are common after 100 units of RBCs have been transfused (total-body iron load of 20 g).
- Preventing this complication by using alternative therapies (e.g., erythropoietin) and judicious transfusion is preferable and cost effective.
- Chelating agents, such as deferoxamine and deferasirox, are available, but the response though is often suboptimal.

Adverse Reactions of Blood Transfusion

INFECTIOUS COMPLICATIONS

Viral infections

1. Hepatitis C virus
2. Human immunodeficiency virus type 1
3. Hepatitis B virus
4. Cytomegalovirus
5. Parvovirus B-19
6. Bacterial contamination

Adverse Reactions of Blood Transfusion

Other infectious agents

- Various parasites, including those causing malaria, babesiosis, and Chagas disease, can be transmitted by blood transfusion.
- Dengue, chikungunya virus, variant Creutzfeldt-Jakob disease, and yellow fever
- Geographic migration and travel of donors shift the incidence of these rare infections.

Adverse Reactions of Blood Transfusion

ALTERNATIVES TO TRANSFUSION

- Autologous blood is the best option when transfusion is anticipated.
- The cost-benefit ratio of autologous transfusion remains high.
- No transfusion is a zero-risk event; clerical errors and bacterial contamination remain potential complications even with autologous transfusions.

TABLE 113-3 Risks of Transfusion Complications

	Frequency, Episodes: Unit
Reactions	
Febrile (FNHTR)	• 1–4:100
Allergic	• 1–4:100
Delayed hemolytic	• 1:1000
TRALI	• 1:5000
Acute hemolytic	• 1:12,000
Fatal hemolytic	• 1:100,000
Anaphylactic	• 1:150,000
Infections[a]	
Hepatitis B	• 1:220,000
Hepatitis C	• 1:1,800,000
HIV-1, -2	• 1:2,300,000
HTLV-I and -II	• 1:2,993,000
Malaria	• 1:4,000,000
Other complications	
RBC allosensitization	• 1:100
HLA allosensitization	• 1:10
Graft-versus-host disease	Rare

[a]Infectious agents rarely associated with transfusion, theoretically possible or of unknown risk include West Nile virus, hepatitis A virus, parvovirus B-19, *Babesia microti* (babesiosis), *Borrelia burgdorferi* (Lyme disease), *Anaplasma phagocytophilum* (human granulocytic ehrlichiosis), *Trypanosoma cruzi* (Chagas disease), *Treponema pallidum*, and human herpesvirus-8.

Abbreviations: FNHTR, febrile nonhemolytic transfusion reaction; TRALI, transfusion-related acute lung injury; HTLV, human T lymphotropic virus; RBC, red blood cell.