Blood products and transfusion

Objectives:

- Introduction.
- Sources of Blood Transfusion
- Blood groups
- Transfusion Triggers
- Blood & Component Transfusion
- Complications of Blood transfusions

Resources:

- Davidson's.
- Slides
- Surgical recall.
- Raslan's notes.

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Once you stop learning
you start dying.

Blood transfusion

- The era of modern blood transfusion began in the early 1900s with discovery of the **ABO red cell antigen system**.
- During world War I, it was known that adding citrate enabled the storage of anticoagulated blood.

Definition: Is the transfer of Blood or Blood Products from one person (Donor) into another Person's Blood (Recipient).

Sources of blood:

1. **Autologous** blood: Using your own blood.
2. Donor (**Allogeneic**) blood: Using someone else's blood.

Blood Donations: Depends on **age** & **health** of the donor.

Blood Collection:

Blood centers are processing more than 90% of the units collected .

- Traditional **allogeneic** (human to human) donation methods still predominate, but increasing use is being made of red cell apheresis technology[1].

Anticoagulants in Blood:

Blood collection bags contain an anticoagulant-preservative of (CPDA-1) :

1. **Citrate** : prevents calcium from triggering the coagulation pathway.
2. **Phosphate**: in the form of 2,3-DPG, gives nutrition to RBCs.
3. **Dextrose**: provides energy to cells.
4. **Adenine** : prolong storability by maintaining ATP to the RBC .

● CPDA-1 ensures a shelf life (24 hours after infusion → viability[2] of at least 70% of the RBCs) of **35** days and hematocrit of 70 to 80% for PRBCs[3]. (The more time passes, the more viability is lost) (hematocrit levels are 45% to 52% for men & 37% to 48% for women).

● **Adsol**, **Nutricel**, **Optisol** are additive solutions which:

1- provide additional nutrients → extending maximum storage to **42** days (for RBCs, so 7 more days were added)

2- ↓**viscosity** → which makes infusion easier.

● If **PRBCs** are freezed immediately once collected, they may stay for **10 years**. Some people donate their own blood for themselves in the future in case they need it (**Autologous** transfusion).

[1] It's a method by which red cells are separated from the blood at the time of collection, with the rest returned to circulation.
[2] The ability to carry O2 from lungs to tissue.
[3] packed red blood cells

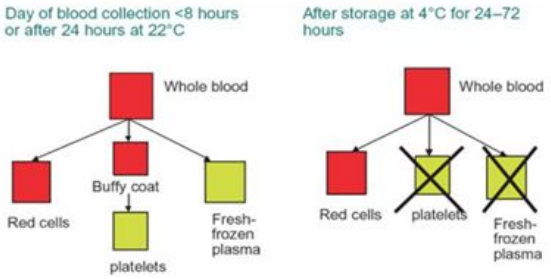
Storage of Blood:

- Storage impairs red cells function. Transfused blood delivers O2 to the tissues less efficiently.

(which means we need to use old blood bags before the new ones, to reduce the amount of wasted blood)

- Refrigerated at **1 to 6°C** (usually **4°C**). Even though, cell metabolism continues and changes occur → (↓ in **pH** and ↓ in the **levels of 2,3-DPG**.)

(Oxygen–Hgb dissociation curve shifts to left → more affinity)

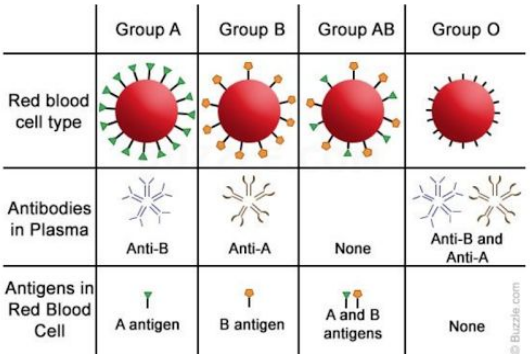


- The deformability of RBCs makes them, over time, more **spherical** and **rigid** → increasing resistance to capillary flow.
- Cell leakage of **Potassium** (≈ **6** mEq/U) → **hyperkalemia.**

Blood typing

Identified red blood cell (RBC) antigens :

- **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**.



Blood Type		Donate Blood To	Receive Blood From
A+	34% 2nd most common	A+ AB+	A+ A- O+ O-
O+	37% most common	O+ A+ B+ AB+	O+ O-
B+	10%	B+ AB+	B+ B- O+ O-
AB+	4%	AB+	Everyone
A-	6%	A+ A- AB+ AB-	A- O-
O-	6%	Everyone	O-
B-	2%	B+ B- AB+ AB-	B- O-
AB-	1%	AB+ AB-	AB- A- B- O-

Blood typing:

- **Forward type:** determines the **ABO** and **Rh** phenotype of the recipient's RBCs by using **antisera** directed against the A, B, and D antigens. (this method is not enough)
- **Reverse type = cross matching** : detects **isoagglutinins**[4] in the patient's serum and should correlate with the ABO phenotype, or forward type. (mix serum of pt with RBCs of donor, and RBCs of pt with serum of donor, separately , and keep them incubated for 24 hours in 37 degree to make sure there's no reaction).
- Rh typing can usually be determined by adding a **commercial reagent (anti-D)** to recipient RBCs.
- Those with type **AB** blood form no ABO group antibodies. (universal recipient).
- Those with type **O** have antibodies against both. (universal donor) - They are always kept in the ER for emergency.

[4] Isoantibody normally present in the serum of an individual that causes the agglutination of the red blood cells of another individual of the same species.

Type & 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 SHOULD be done** by mixing recipient serum with donor RBCs as a final compatibility test prior to transfusion.

Crossmatch:

Done using a **Coombs test**[5] (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 Ab screen.

Blood and Products Transfusion. Why?

● Increase **oxygen carrying capacity** (Hb must be >7 g/dL) .
● Restoration of red cell mass.
● Correction of bleeding caused by **platelet dysfunction**.
● Correction of bleeding caused by **factor deficiencies**. (hemophilia, von-willebrand, liver disease).
We should give the pt these factors with the transfusion.
● correction of anemia.

How much blood do we need to give?

Oxygen Delivery:

- **Oxygen Delivery (DO_2)** is the oxygen that is delivered to the tissues.
- **DO_2= CO x CaO_2**
- **Cardiac Output (CO)** = HR x SV
- **Arterial Oxygen Content (CaO_2)** : the amount of oxygen bound to hemoglobin plus the oxygen dissolved in plasma.
- **CaO_2 = (Hgb x 1.39 x SaO_2)**[6] **+ (PaO_2 x 0.003)**[7]
    - **Hgb** is the main determinant of oxygen content in the blood.

Which means that we can't change saturated or dissolved O_2, but we can increase Hb.

- 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 of blood in theater:

- Legal Aspects:
    - Two qualified personnel check it at the bedside to prevent a potentially fatal clerical error.
    - **Recipient (ID)** & **unit identification** , confirmation of compatibility, expiration date.
    - 60% of transfusions occur perioperatively.
    - Responsibility of transfusing perioperatively is with the **anesthesiologist.**
- Urgent transfusion situations require flow rates faster than gravity can provide:

1. **Pressure bags** that completely encase the blood bag and apply pressure evenly to the blood bag surface (see the picture in the right).
2. If external pressure is anticipated → **large-bore needles** are recommended for venous access to prevent hemolysis.
3. If only a **small-gauge needle** is available → the transfusion may be diluted with normal saline , but this may cause unwanted volume expansion. (lactate ringer should not be used with the blood transfusion because it may lead to clotting.)

[5] A blood test which is done by adding antigens to a blood sample and see the reactions to determine ABO incompatibility.
[6] 1.39 is the amount of O2 carried by each gram of Hb. It is constant.
[7] 0.003 is the amount of dissolved O_2 in plasma.

MANAGEMENT: determinant factors:

1. Age (e.g. if the pt is a child → don't give him adult's blood bag cuz it'll lead to volume overload. If the pt is an elderly → don't give him blood too fast or overload will occur)
2. Severity of symptoms.
3. Cause of the deficit.
4. Underlying medical condition.
5. Ability to compensate for decreased oxygen-carrying capacity.
6. Tissue oxygen requirements are all considered.

Clinical evaluation:

1. Appearance (pallor, diaphoresis[8])
2. Mentation (alert, confused)
3. Heart rate
4. Blood pressure
5. Nature of the bleeding (active, controlled, uncontrolled).
    - Active = stop bleeding, controlled = adjust it, uncontrolled = give more blood.
    - For Each **500 ml blood loss Hb will drop 1 gram**.
    - People **can't** tolerate losing more than 20% of blood.

Laboratory evaluation:

1. Hgb.
2. Hematocrit.
3. Platelets.
4. Clotting function (coagulation profile).

When to transfuse? (indication)

- TRICC **(Transfusion Requirements in Critical Care)** trial, demonstrated that in the critical care setting, a transfusion threshold of **7** g/dL of Hb was as safe as a threshold of **10** g/dL.
    - Patient can compensate with Hb as low as 7 g/dL, if he reaches it give him blood, if he is above it you don't need to give him.
    - Healthy pt can compensate with low Hb. (6 or 7 g/dL). IHD pt **can't**.
    - 10g/dL is mandatory for IHD.

  So don't transfuse til Hb is 7 g/dL (or 10 g/dL in IHD pts)
- A subgroup analysis generated some concern that patients with **ischemic heart disease (IHD)** benefit from higher transfusion threshold (IHD may render patients more intolerant of anemia, they can't tolerate low Hb levels because their coronaries are blocked)

[8] Sweating large amounts

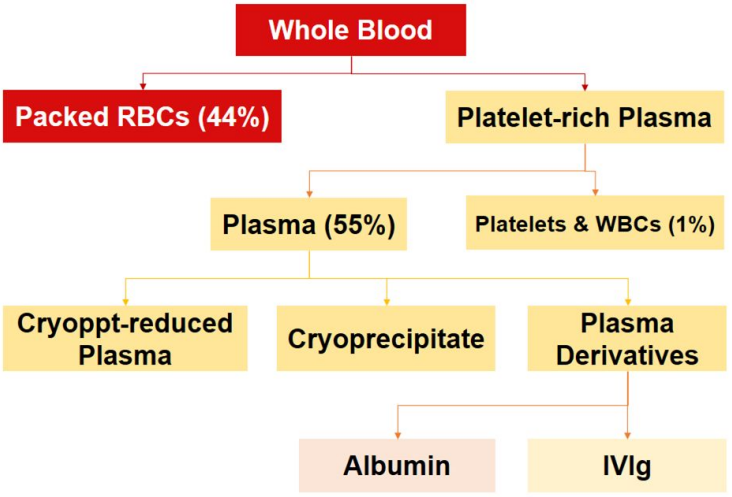
Blood components

- **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 **whole blood is rarely used**.
- The more components the more chances of allergies and reactions.

➔ **Fresh frozen plasma** = contains all coagulation factors.

➔ **Cryoprecipitate** = contains fibrinogen and some other factors.

➔ If you give pt more than 4 units of blood, you should give for each unit FFP, platelets & cryoprecipitate (critical for preventing DIC)



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	$5.5x10^{10}$/RD unit	Increase platelet count 5000-10,000 µL
	200-400	≥ $3x10^{11}$/SDAP product	CCI ≥ $10x10^{9}$/L within 1h and ≥ $7.5x10^{9}$/L within 24 h post-transfusion
FFP	200-250	Plasma proteins , coagulation factors , protein C and S , antithrombin	Increase coagulation factors about 2%
Cryoprecipitate	10-15	Cold – insoluble plasma proteins fibrinogen , factor VIII , vWF	Topical fibrin glue , also 80 IU factor VIII

Packed red blood cells	• 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 • Physicians would still transfuse a patient with ongoing hemorrhage & unstable vital signs despite adequate fluid resuscitation, & would occasionally consider withholding transfusion for Hgb levels even lower than 6 g/dL in a young, healthy, asymptomatic patient without ongoing hemorrhage. • 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 IV line **with normal saline.**(should be isotonic 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 unit unrefrigerated for **more than 30 minutes** is discarded. **NEVER** mixed with: • **Lactated Ringer's solution** can lead to clotting due to the added calcium **(give in another line.)** • Calcium; may cause clumping or clots • Dextrose (Hypotonic); may cause hemolysis or clumping • Medication • Hypertonic solutions
Fresh Frozen Plasma	• A unit of FFP typically has a volume of 200 to 250 mL, **must be ABO compatible** , and should be given through blood tubing within 2 to 6 hours of thawing[9]. • 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.** • FFP is used when there are multiple coagulation factor deficiencies[10](e.g. disseminated intravascular coagulation >HOW !![11]) and also hemophilia. • FFP should not be used to correct prolonged clotting times in patients who are not bleeding or who are not about to undergo immediate surgery.
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). Each unit will increase plasma from **5,000 - 10,000/µL** (very important! Usually comes in MCQs! See it in table 113-2). • In children it is 1U/10kg body weight. • Platelet concentrates are indicated in thrombocytopenia, when platelet function is defective, and in patients receiving massive blood transfusions when there is microvascular bleeding (oozing from mucous membranes, needle puncture sites and wounds). • Platelets can't be kept in the fridge (can't be frozen).
Cryoprecipitate	• Cryoprecipitate is a source of fibrinogen, **factor VIII**[12] , and von Willebrand factor (vWF). • It is ideal for supplying fibrinogen to the 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.

[9] Thawing: putting the blood bag in a warm water - after getting it out of the fridge - till it restores its liquid form (إذابة).
[10] Also, single clotting factor deficiency is usually treated by FFP.
[11] **DIC**: imbalance b/w ↓ breaking clots and ↑↑forming new clots. >> spread clots which depletes platelets and clotting factors causing excessive bleeding.
[12] Deficiency in this factor → hemophilia A

Recall :

Which electrolytes is most likely to fall with infusion of stored blood? And Why?
Ionized calcium ; the citrate preservative used for storage of blood binds serum calcium.
What changes occur in the storage of PRBCs?
Decrease in Ca++ , 2,3-DPG and PMN.
Increase in K+ and H+ (reduce PH)
What is the thrombocytopenia?
Low platelet count (less than 100,000).
How much one unit of PRBCs will increase hematocrit?
Hematocrit is Hb level x 3 → about 3-4%
What are common causes of thrombocytopenia in surgical patient?
Sepsis, H2 blockers, heparin, massive transfusion , DIC, antibiotics , spurious lab value, Swann-Ganz catheter.
What common medication could cause irreversible platelet dysfunction?
Aspirin (inhibits cyclooxygenase)**.**
What can be given to help correct platelet dysfunction from uremia , aspirin or bypass?
DDAVP (desmopressin)
What are general guidelines for blood transfusion?
Acute blood loss, Hb less than 10 with COPD or CAD, or healthy symptomatic patient with Hb less than 7.
Why not infuse lactated ringer's (LR)?
calcium in LR may result in coagulation within IV line.
For how long packed RBCs stored?
about 6 weeks (42 days).
What is the most common cause of transfusion reaction?
ABO incompatibility as result of clerical error.
What are the symptoms of hemolytic transfusion reaction?
Fever, chills, nausea , vomiting , hypotension, lumbar pain, chest pain, abnormal bleeding.
What is the treatment for transfusion hemolysis?
Stop transfusion, provide fluids, perform diuresis by lasix to protect kidneys, alkalinize urine (bicarbonate) and give pressors as needed
What component of blood can cause fever? WBCs
When should aspirin administration be discontinued preoperrativly?
At 1 week because platelets live 7 to 10 days (must use judgment if patient at risk for MI, stroke because it may be better to continue and use excellent surgical hemostasis in these patients.
What can move the oxyhemoglobin dissociation curve to the right?
Acidosis, 2,3- DPG, fever, elevated PCO2 (to the right means greater ability to release the O2 to the tissues.
What is the normal of RBC and platelet?
RBCs :120 days.
Platelets : 7-10 days.
What are the the coagulation factor deficient in hemophilia A and B?
Hemophilia A : factor 8
Hemophilia B : factor 9
How hemophilia A and B inherited? sex linked recessive
What is the preoperative treatment of hemophilia A? Factor 8 infusion
What is willebrand's disease inherited?
Is autosomal dominant disease which is caused by deficiency in von willebrand factor (vWF) and factor VIII:C.
What is used to correct willebrand's disease? DDAVP or cryoprecipitate
What coagulation study is abnormal in hemophilia A, B and willebrand's disease?
Hemophilia A : elevated PTT.
Hemophilia B : elevated PTT.
Willebrand's disease : elevated bleeding time
What is the effect of deficiency in protein C, protein S or antithrombin III? Hypercoagulable state.
What is the most common inherited hypercoagulable state? Factor V leiden

Adverse Reactions of Blood Transfusion

- The most common reactions are not life threatening (clinical errors usually, e.g. didn't double check the file name), **although serious reactions can present with mild symptoms and signs** .
- Reactions can be reduced or prevented by modified (filtered, washed, or irradiated) blood components, especially with pts with multiple blood transfusions.

IMMUNE-MEDIATED REACTIONS:

Acute hemolytic transfusion reactions (AHTR):

- 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.
- AHTR presents as hypotension, tachypnea, tachycardia, fever, chills, hemoglobinemia, hemoglobinuria, chest and/or flank pain (if pt is awake), and discomfort at the infusion site.
  – If any patient is awake and feels chest pain, **stop transfusion immediately**.
- 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).
3. Indirect bilirubin levels.

4- Coagulation studies like prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, & platelet count should be monitored in patients with hemolytic reactions.

Treatment: (stop transfusion → treat symptoms & send a sample to lab)

- 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.
- 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.

Allergic reactions:

- Urticarial reactions[13] 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).

Anaphylactic reaction:

- It's the most **severe** reaction.
- The pt won't react in the first time, but in the 2nd time he/she will severely react.
- 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.
- Management: 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.

[13] formation of pruritic (itchy), raised, red-rimmed wheals - انتفاخات - on the skin due to histamine release.

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 & cannot be eliminated by an immunodeficient host.
- Mediated by donor's T lymphocytes that recognize host HLA antigens as foreign & mount an immune response
- Manifested clinically by fever, a characteristic cutaneous eruption, diarrhea, & liver function abnormalities.

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 (complications).

NONIMMUNOLOGIC REACTIONS:

Fluid overload	Electrolyte toxicity	Hypothermia	Iron overload
- Blood components are excellent volume expanders, & transfusion may quickly lead to volume overload. - Monitoring the rate and volume of the transfusion and using a diuretic can minimize this problem.	-RBC leakage during storage increases the concentration of K^+ in the unit. - Citrate, commonly used for anticoagulation, hold the calcium and thereby inhibits the coagulation cascade. - hypocalcemia[14] may result from multiple rapid transfusion. - Citrate is quickly metabolised to bicarbonate, calcium infusion is seldom required in this setting.	-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.	- 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 (e.g. thalassemia)). - Preventing this complication is 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.

[14] manifestations: circumoral numbness and/or tingling sensation of the fingers and toes.

INFECTIOUS COMPLICATIONS:

1- Viral infections :

- Hepatitis C virus.
- Human immunodeficiency virus type 1
- Hepatitis B virus
- Cytomegalovirus.
- Parvovirus B-19

2- Bacterial contamination.

3- 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.

ALTERNATIVES TO TRANSFUSION: none “for now” :(.

- 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.