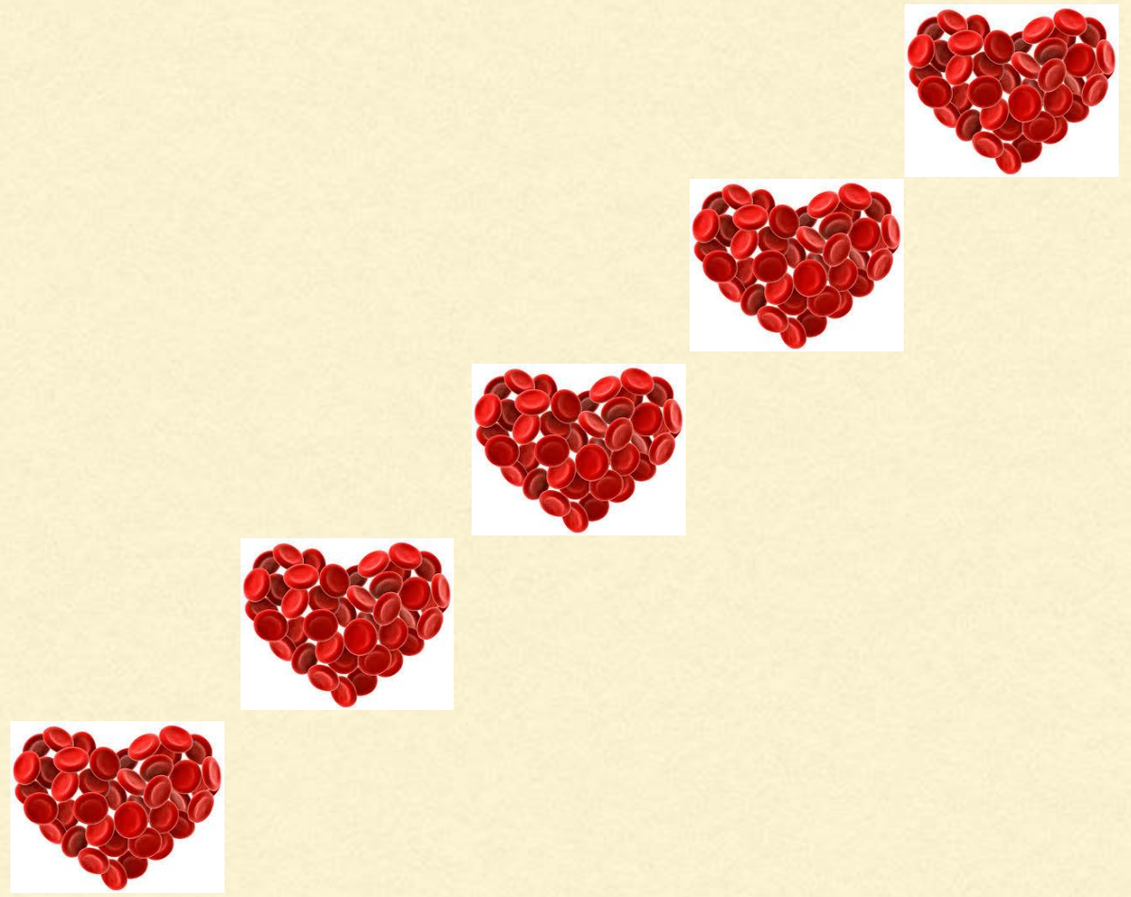
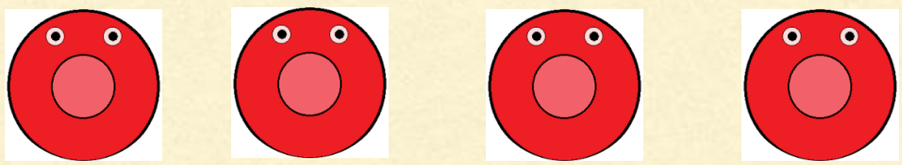


BLOOD TRANSFUSION

Kwannut Srikala , MD
Pediatric Hematologist
Sappasithiprasong Hospital



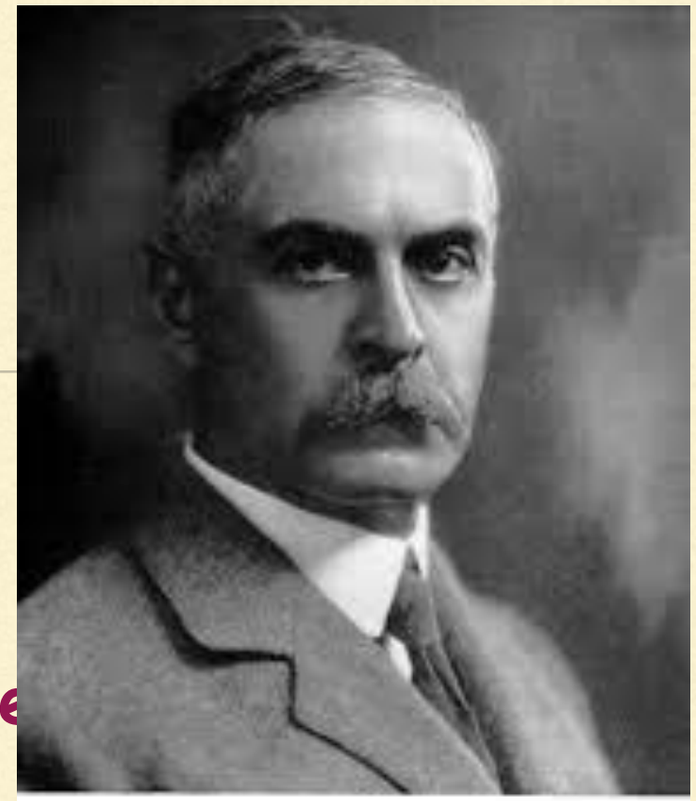
Outline

- Donor & Recipient testing and compatibility
  - "Types", "Crosses" & "Screens"
- Blood Products
  - Where do they come from?
  - What are my option ?
- Ordering blood products like a professional
- Transfusion Complications
- Transfusion recommendations

Pre-transfusion compatibility testing

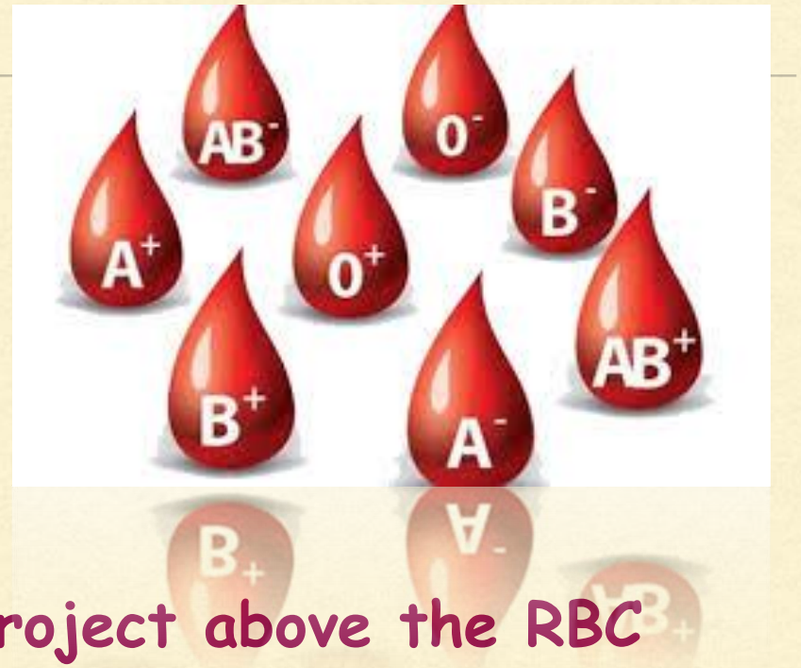
- **Type & Screen:** (low probability of transfusion) **"Type and Hold"**
  - ABO and Rh type
  - Antibody screen
  - Antibody identification
  - DAT
- Type & Crossmatch : (high probability of transfusion)
  - Above steps plus Crossmatch
  - Specific unit(s) set aside for up to three days for a particular patient

Blood Grouping System



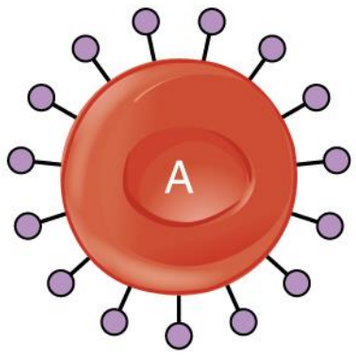
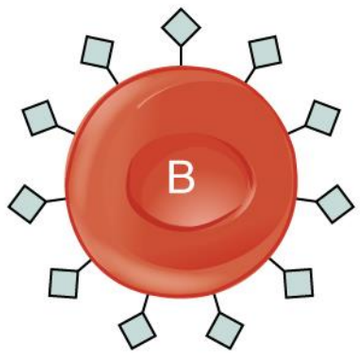
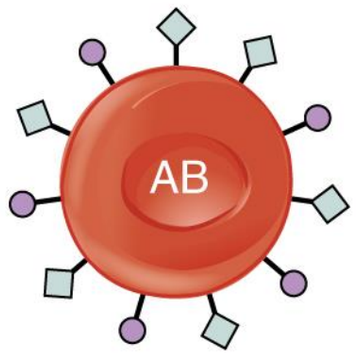
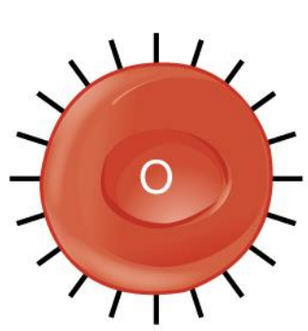
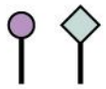
- ABO blood grouping system
  - First described in 1900, by Karl Landsteine
  - Nobel Prize in 1930
- Other systems:
  - Rh (D,C, c, E, e)
  - Lewis
  - Kell
  - Kidd
  - Duffy
  - etc

ABO Blood Group System

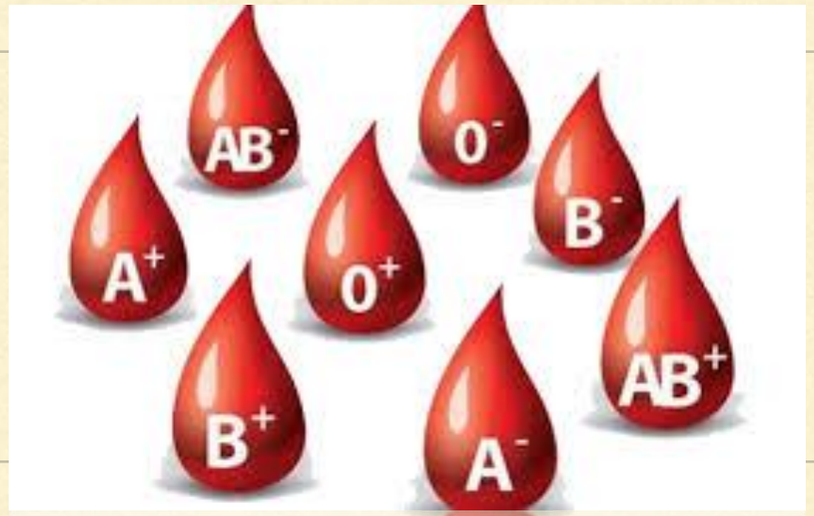


ABO system:

- **Blood types: O, A, B, and AB.**
  - **Frequencies vary with ethnicity.**
- **Antigens of the ABO blood group**
  - **ABO antigens are oligosaccharide chains that project above the RBC surface.**
  - **ABO gene locus has 3 allelic forms:**
- **A and B alleles code for glycosyltransferases**
- **O allele encodes aninactive glycosyltransferase**
- **Function of these antigens are not known.**

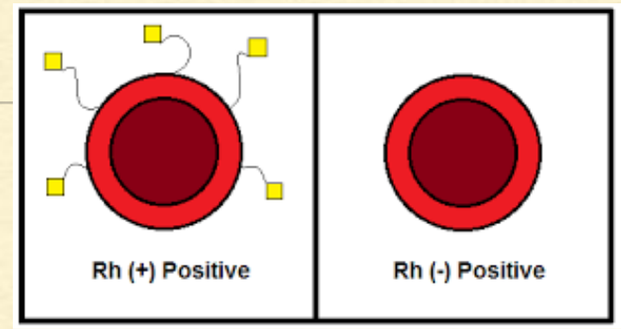
	Blood Type			
	A	B	AB	O
Red Blood Cell Type				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in Red blood Cell	 A antigen	 B antigen	 A and B antigens	None
Blood Types Compatible in an Emergency	A, O	B, O	A, B, AB, O (AB^+ is the universal recipient)	O (O is the universal donor)

Natural Alloantibodies



- In individuals that lack A and/or B antigen on the red cells, their plasma will contain naturally-occurring antibodies to the missing antigen(s).
- Thus:
  - Group A individuals will have anti-B antibodies
  - Group B individuals will haveanti-A antibodies
  - Group O individuals will have both anti-A and anti-B antibodies
  - Group AB individuals will have neither anti-A nor anti-B
- antibodiesThese antibodies naturally appear in the blood by four to six months of age.

The Rh (Rhesus) blood group system



- second most important blood group system
- severe hemolytic transfusion reactions and most hemolytic disease of the fetus and newborn (HDFN) cases are associated with antibodies to the Rh group antigens
- The Rh system consists of over 50 red cell antigens.
- There are 5 main Rh red cell antigens : D, C, c, E, e that involve most clinically significant transfusion complications

The Rh (Rhesus) blood group system

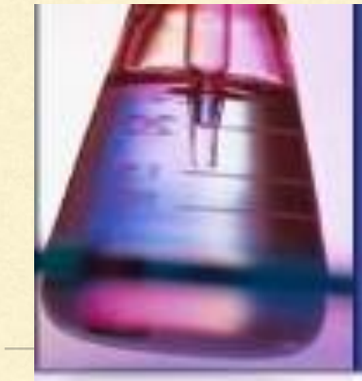
- Two separate genes for the Rh system are found on chromosome 1.
- One gene, RHD, encodes for the D antigen.
  - Individuals with the D antigen present on their red blood cells are labeled as "Rh (D)–positive."
  - Those who do not have the D antigen are labeled as "Rh (D)–negative.
- A second gene, RHCE, encodes for a combination of CE or ce antigens together.
  - RHD and RHCE are highly homologous to each other.
  - In essence, RHCE is the original gene, and RHD is a duplication of RHCE.

Pre-transfusion compatibility testing

- Type & Screen: (low probability of transfusion) "Type and Hold"
  - ABO and Rh type
  - Antibody screen
  - Antibody identification
  - DAT
- Type & Crossmatch : (high probability of transfusion)
  - Above steps plus Crossmatch
  - Specific unit(s) set aside for up to three days for a particular patient

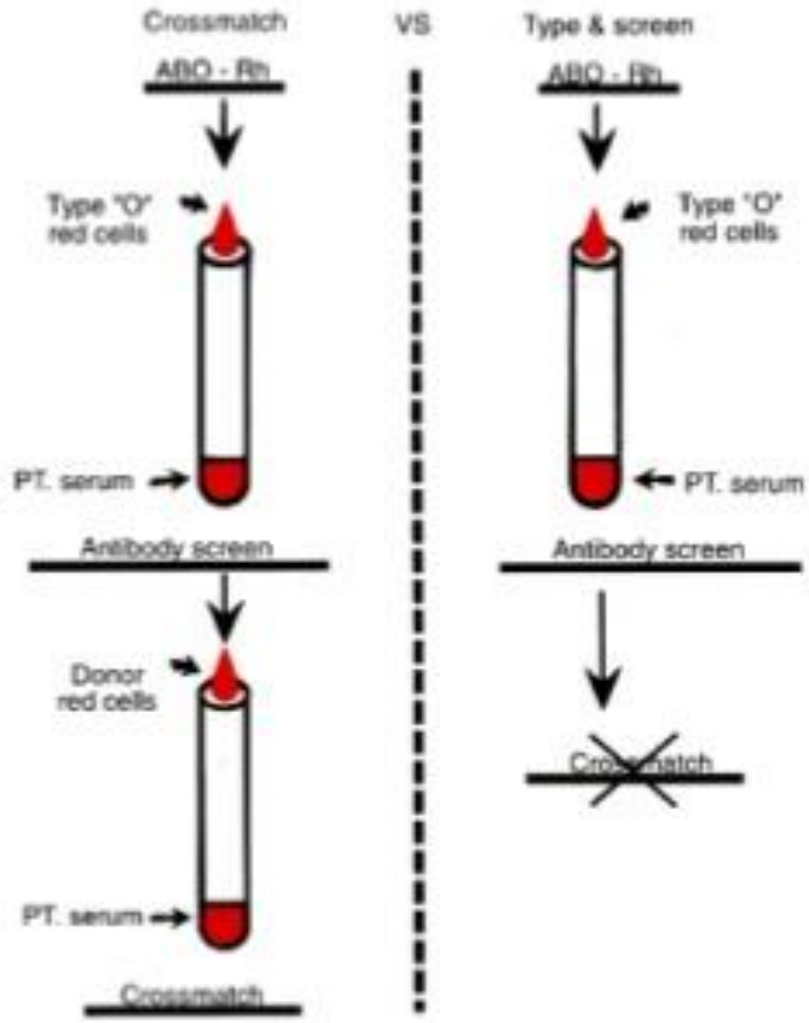
Antibody screen

- An RBC antibody screen is used to screen an individual's blood for antibodies directed against red blood cell (RBC) antigens other than the A and B antigens.
- The primary reason that a person may have RBC antibodies circulating in the blood is because the person has been exposed, through blood transfusion or through pregnancy, to RBCs other than his or her own (foreign RBCs).
- These antibodies have the potential to cause harm if a person is transfused with red blood cells that the antibodies may target



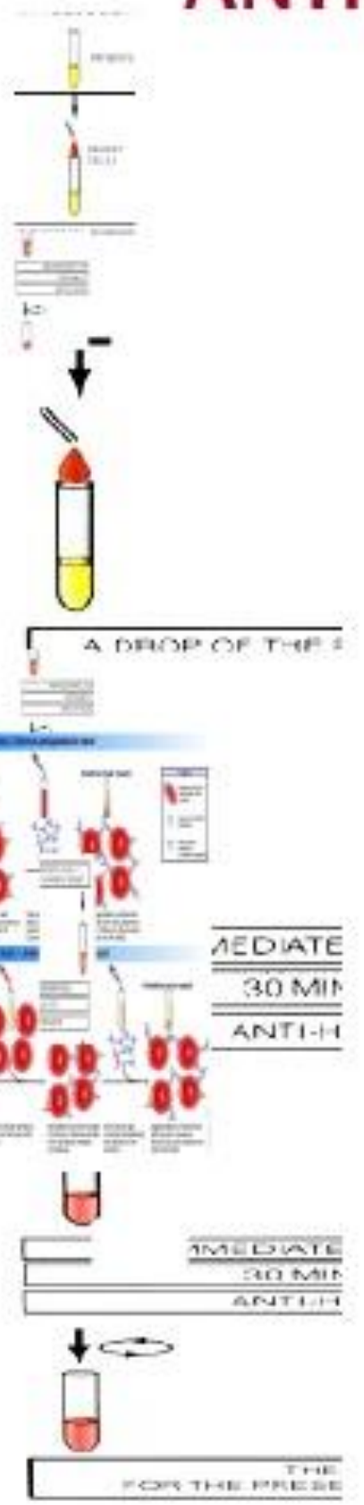
Antibody screening

- The purpose of antibody screening is to detect RBCs antibodies other than anti-a and anti-B (also called unexpected antibodies).



ANTIBODY SCREEN

patient serum



patient serum

reagent RBC number 1

reagent RBC number 2

AHG

AHG

no agglutination (negative test)

agglutination (positive test)

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Antibody identification

- If an antibody is detected, then an antibody identification test must be done to determine which antibodies are present.

- During a crossmatch, a variation of the RBC antibody screen is performed if clinically significant antibodies are present.

- In the case of blood transfusions, RBC antibodies must be taken into account and donor blood must be found that does not contain the antigen(s) to which the person has produced antibodies.

Antibody screen

	Rh	C	c	D	E	e	C^w	M	N	S	s	P1	K	Lea	Leb	Fya	Fyb	Jka	Jkb	IAT
1	R_1R_1	+	-	+	-	+	-	-	+	-	+	+	-	+	-	+	-	-	+	-
2	R_2R_2	-	+	+	+	-	-	-	+	-	+	-	+	-	+	+	-	+	-	-
3	rr	-	+	-	-	+	-	+	-	+	-	+	-	-	+	-	+	+	-	+

Antibody identification panel

	Rh	C	c	D	E	e	C^w	M	N	S	s	P1	K	Lea	Leb	Fya	Fyb	Jka	Jkb	IAT	Enz
1	$R_1^wR_1$	+	-	+	-	+	+	+	-	+	-	+	-	+	-	-	+	-	+	+	-
2	R_1R_1	+	-	+	-	+	-	+	+	+	+	-	+	-	+	+	-	+	-	+	-
3	R_2R_2	-	+	+	+	-	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-
4	r'r	+	+	-	-	+	-	-	+	-	+	+	-	-	+	-	+	-	+	-	-
5	r''r	-	+	-	+	+	-	+	+	+	+	+	-	-	+	+	-	+	-	+	-
6	rr	-	+	-	-	+	-	-	+	-	+	-	-	-	+	-	+	-	+	-	-
7	rr	-	+	-	-	+	-	-	+	-	+	+	+	+	-	-	+	+	-	-	-
8	rr	-	+	-	-	+	-	+	-	+	-	+	-	-	+	+	-	-	+	+	-
9	rr	-	+	-	-	+	-	+	-	-	+	-	-	-	-	+	-	-	+	+	-
10	rr	-	+	-	-	+	-	-	+	+	-	+	+	-	+	+	-	-	+	-	-

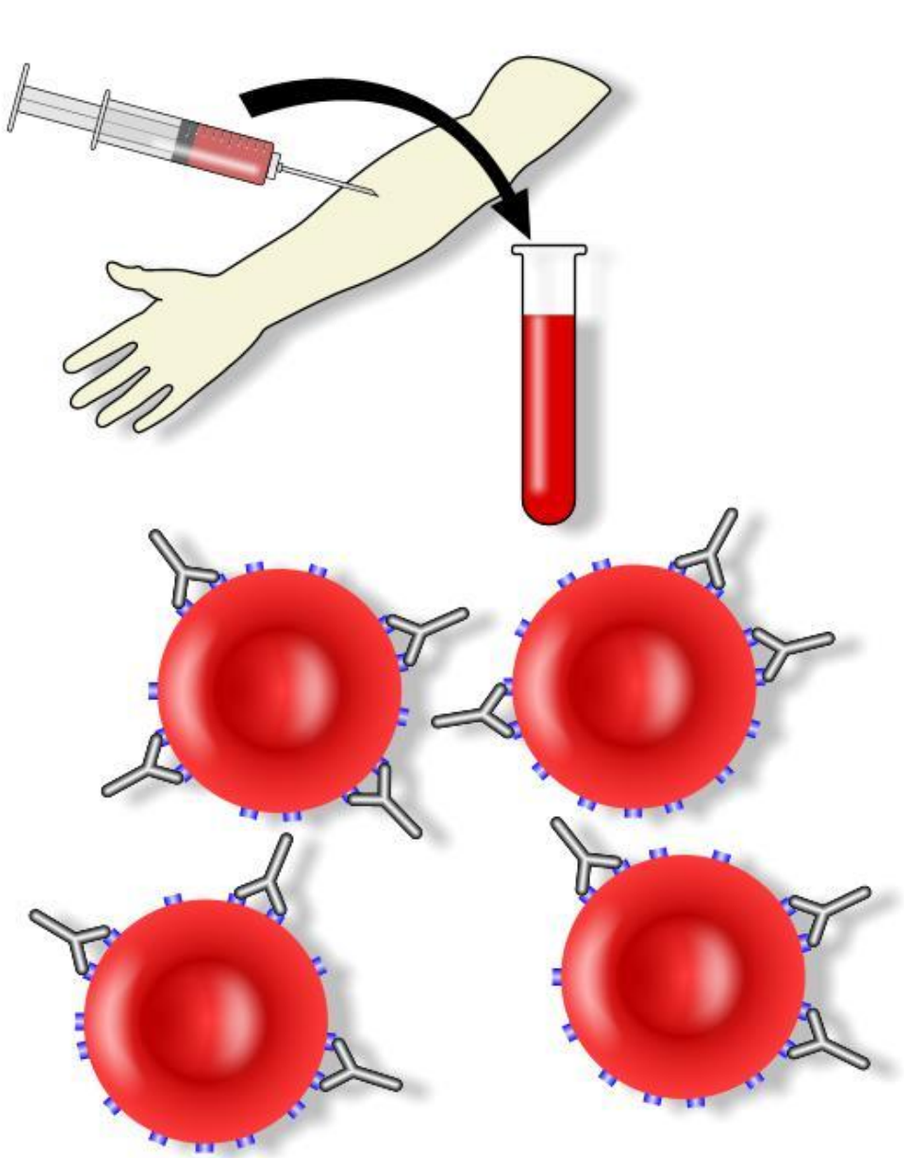
Pre-transfusion compatibility testing

- **Type & Screen:** (low probability of transfusion) **"Type and Hold"**
  - **ABO and Rh type**
  - **Antibody screen**
  - **Antibody identification**
  - **DAT/IDCT**
- **Type & Crossmatch : (high probability of transfusion)**
  - **Above steps plus Crossmatch**
  - **Specific unit(s) set aside for up to three days for a particular patient**

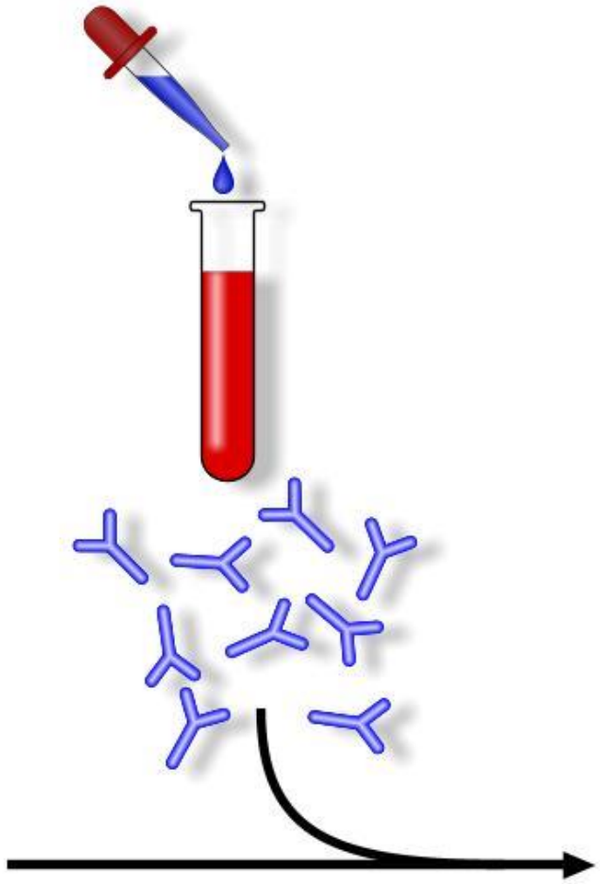
Direct Coombs Test

- used to detect if antibodies or complement system factors have bound to RBC surface antigens in vivo.
- A blood sample is taken and the RBCs are washed and then incubated with antihuman globulin.
- If this produces agglutination of RBCs, the direct Coombs test is positive, a visual indication that antibodies are bound to the surface of red blood cells.

Direct Coombs test / Direct antiglobulin test

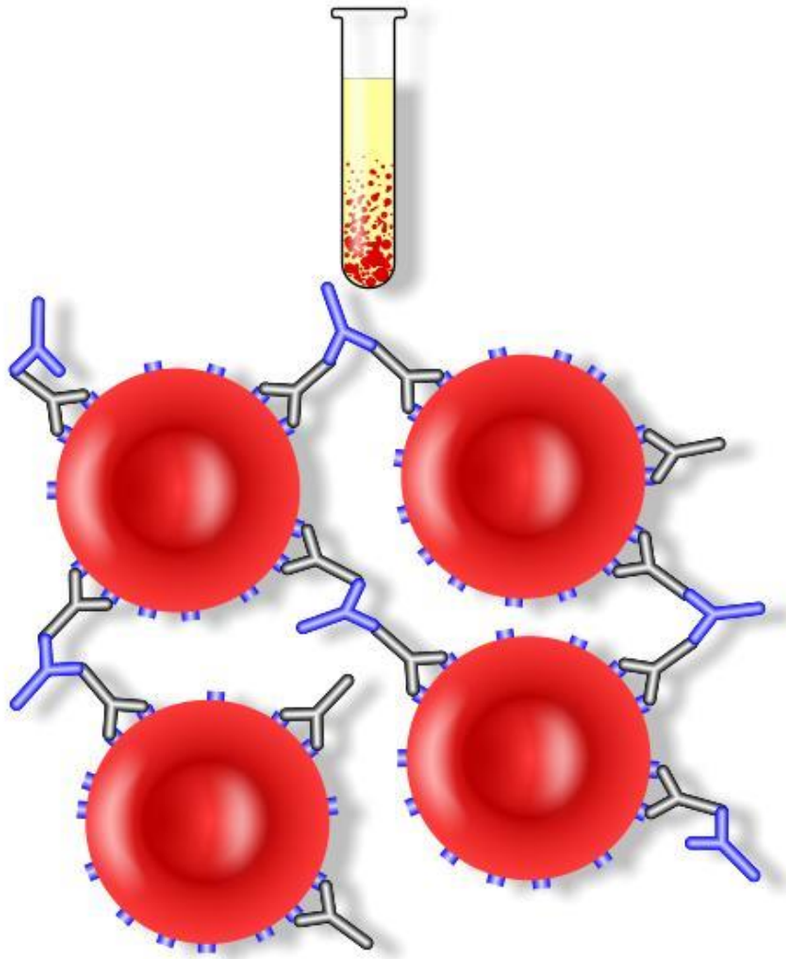


Blood sample from a patient with immune mediated haemolytic anaemia: antibodies are shown attached to antigens on the RBC surface.



The patient's washed RBCs are incubated with antihuman antibodies (*Coombs reagent*).

Positive test result



RBCs agglutinate: antihuman antibodies form links between RBCs by binding to the human antibodies on the RBCs.

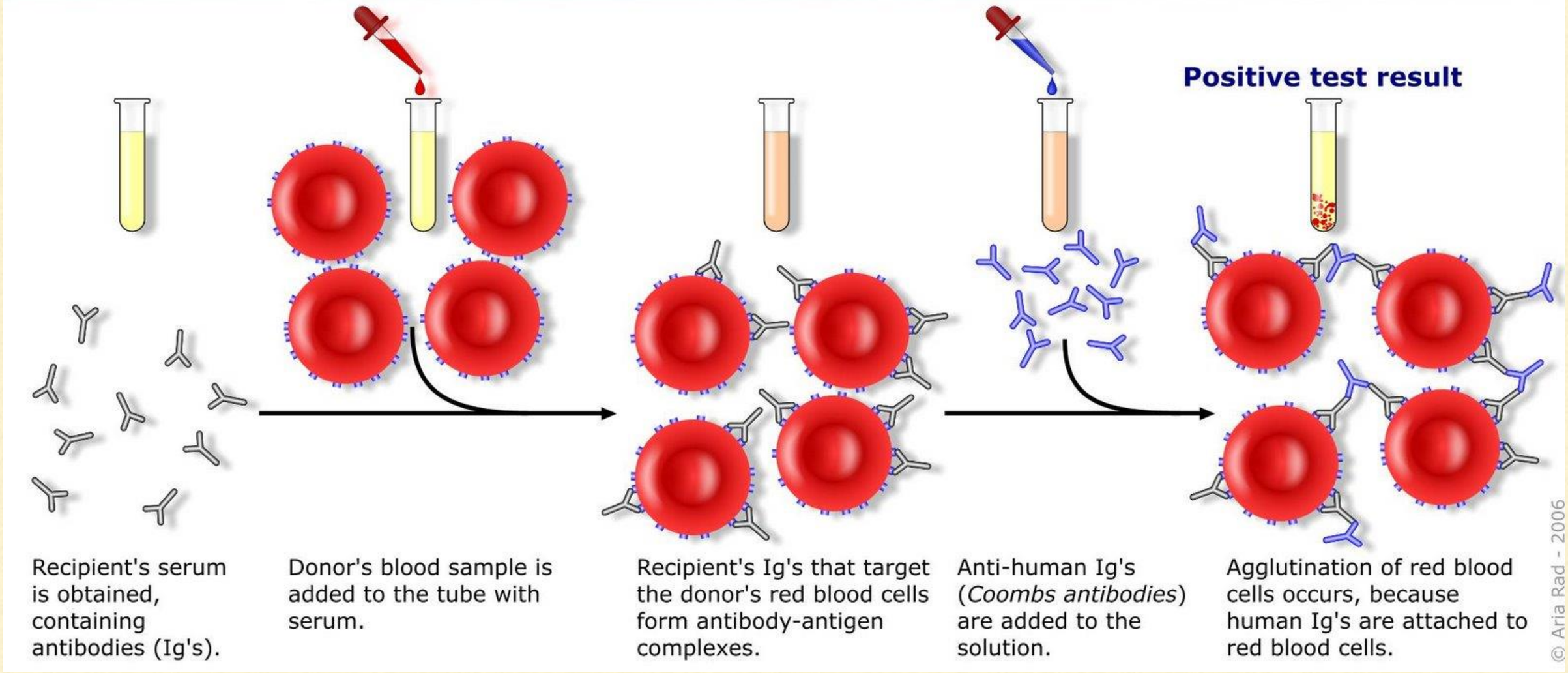
Indirect Coombs Test

- The indirect Coombs test (indirect antiglobulin test or IAT) is used to detect in-vitro antibody-antigen reactions.

- It is used to detect very low concentrations of antibodies present in a patient's plasma/serum prior to a blood transfusion.

- The IAT can also be used for compatibility testing, antibody identification, RBC phenotyping, and titration studies

Indirect Coombs test / Indirect antiglobulin test



Pre-transfusion compatibility testing

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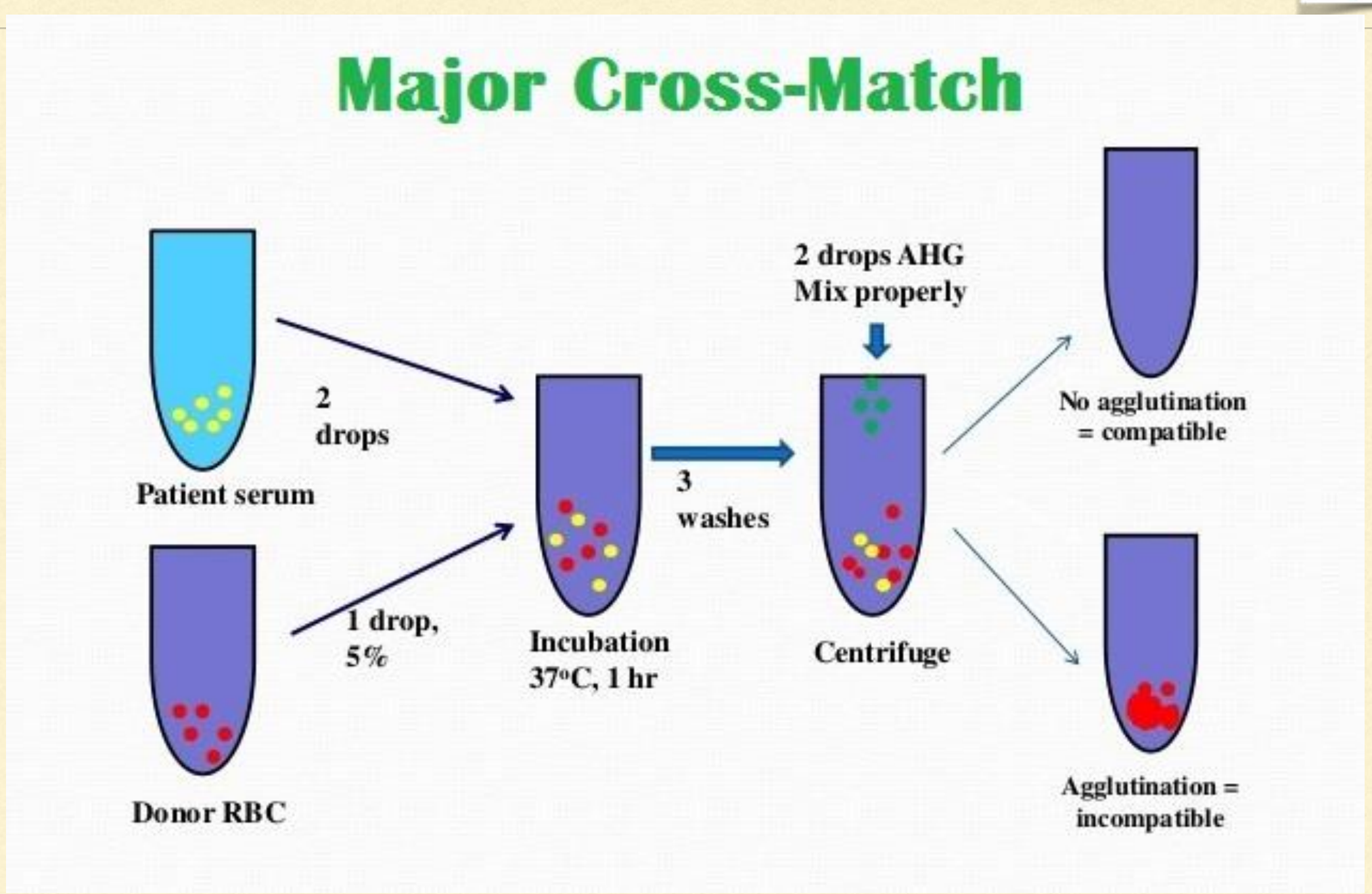
Principle

- Cross-matching will detect incompatibilities between the donor and recipient
- There are two types of cross-matches:
  - The **major crossmatch** involves testing the patient's serum with donor cells to determine whether the patient has an antibody which may cause a hemolytic transfusion reaction or decreased cell survival of donor cells. This is the most important cross-match.
  - The **minor crossmatch** involves testing the patients cells with donor plasma to determine whether there is an antibody in the donor's plasma directed against an antigen on the patient's cells.

Pre-transfusion Compatibility Testing



Purpose of Cross Matching

- The crossmatch is routinely used as the final step of pretransfusion compatibility testing.

- The crossmatch will detect the following:

1. Most recipient antibodies directed against antigens on the donor red blood cells.

2. Major errors in ABO grouping, labeling, and identification of donors and recipients.

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  - Where do they come from?
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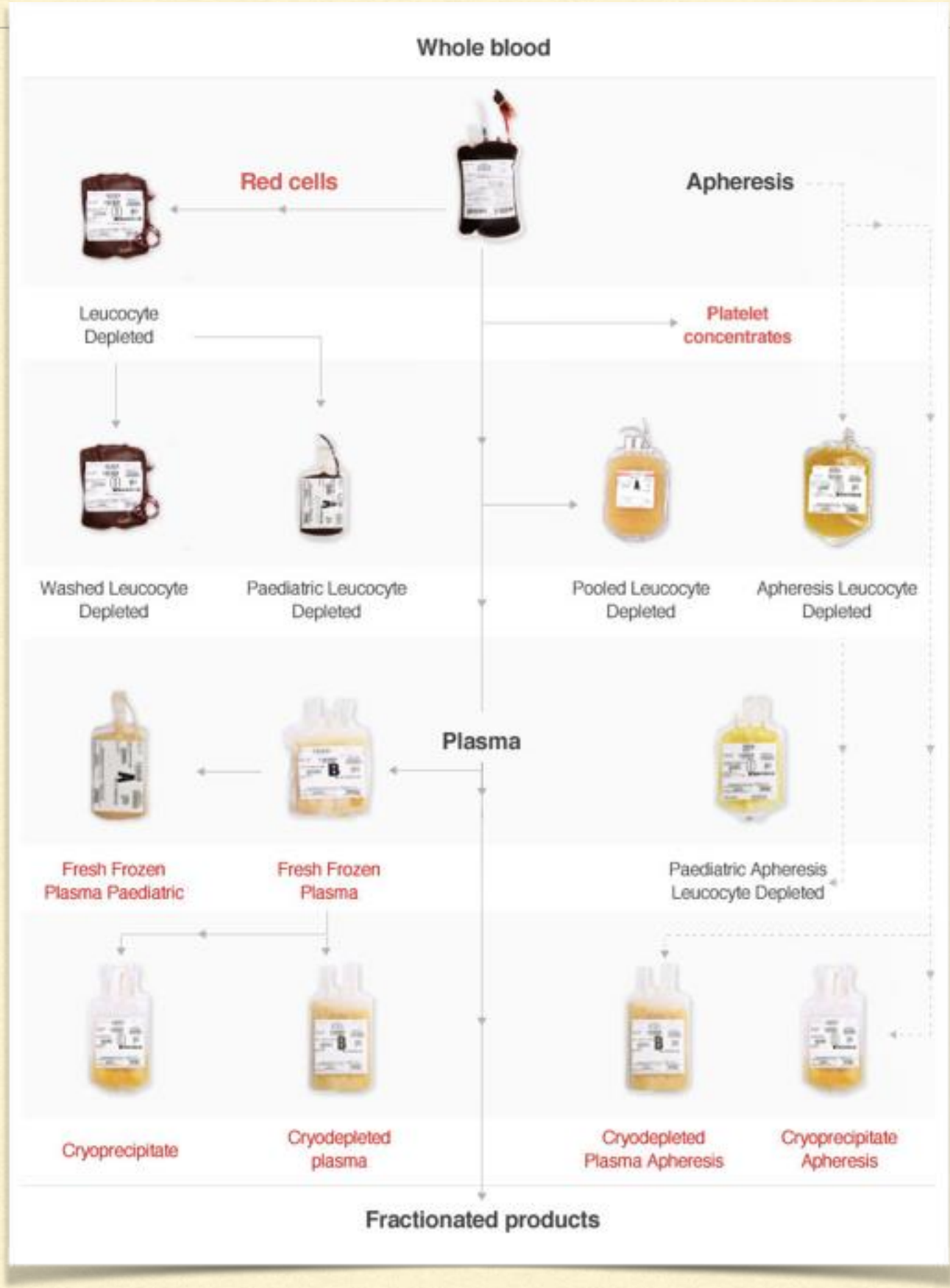
- Transfusion Complications
- Transfusion recommendations


Whole blood
Red cells
Apheresis
Leucocyte Depleted
Platelet concentrates
Washed Leucocyte Depleted
Paediatric Leucocyte Depleted
Pooled Leucocyte Depleted
Apheresis Leucocyte Depleted
Plasma
Fresh Frozen Plasma Paediatric
Fresh Frozen Plasma
Paediatric Apheresis Leucocyte Depleted
Cryoprecipitate
Cryodepleted plasma
Cryodepleted Plasma Apheresis
Cryoprecipitate Apheresis
Fractionated products

Where do they come from?

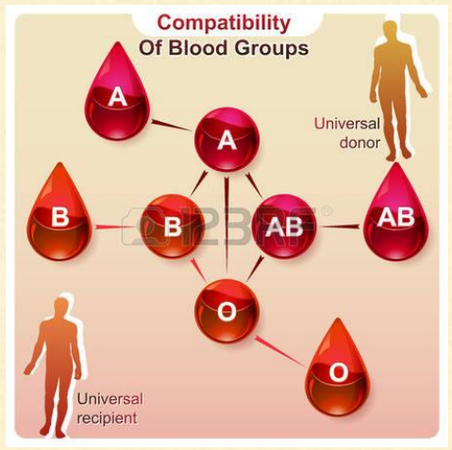
Donors screened:

- Risk factors for transmissible infectious agents
- Health assessment for minimum physiologic criteria

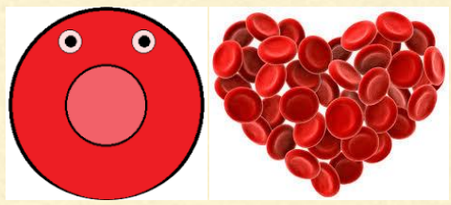
Serologic Testing of donor blood

- Donor's ABO group and Rh type
- Syphilis negative
- Nonreactive for antibodies to
  - humanimmunodeficiencyvirus(anti-HIV-1/2)
  -hepatitis C virus(anti-HCV)
  -human T-cell lymphotropic virus(anti-HTLV-I/II)
  -hepatitis B core antigen(anti-HBc)& hepatitis B surface antigen (HBsAg).
- Negative nucleic acid tests for:
  -HCVribonucleicacid(RNA)
  -HIV-1RNA
  -WestNilevirus(WNV

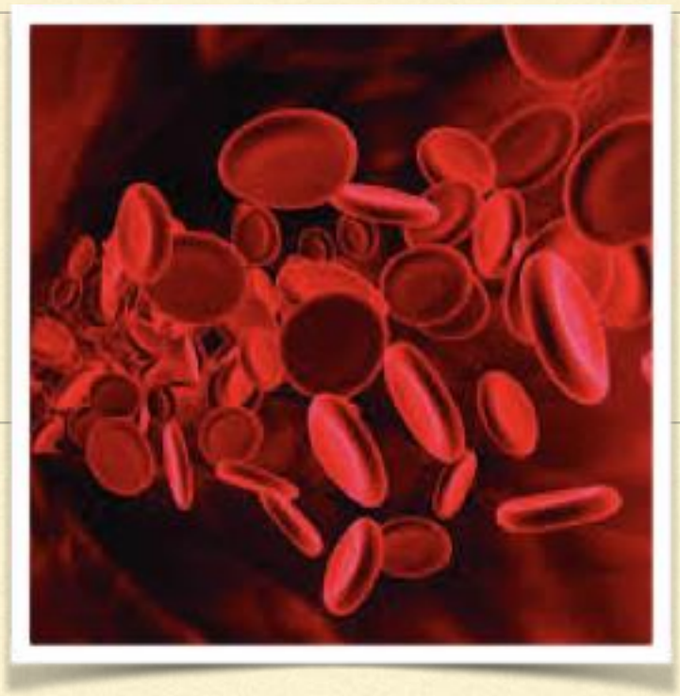
Packed Red Blood Cells



- Estimated unit size = 250 to 350ml
- Average hematocrit of a unit is ~65 to 75%
  - Remember it is 'packed' or concentrated
- mixed with preservative
  - CPDA-1: shelf life of ~35 day
    - Citrate, Phosphate, dextrose, adenine
  - AS-1: shelf life for ~42 days
    - Adsol ®
    - Adenine, dextrose, sorbitol, and manitol



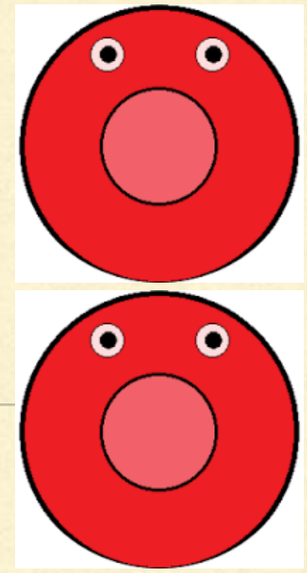
Indications for PRC



Increase oxygen-carrying capacity.

- symptomatic anemia
- red cell exchange transfusion

PRC Modifications



- Leukoreduction
  - WBCs removed via filtration
  - Removes 99.9%
- Adverse effects reduced following Leukoreduction

-Febrile nonhemolytic transfusion reaction
-HLA alloimmunization
-Reduced transmission of infectious agents that are harbored in WBCs....most notably CMV
-Decreases but does not prevent transfusion associated graft versus host disease – ONLY 99.9% reduction

PRC Modifications

Irradiation

-Gamma irradiation of the blood product to stop proliferation of donor lymphocytes

Remember only99.9% are removed with leukoreduction

-Prevents transfusion-associated graft-vests-host-disease

100% fatal complication!!!

Indicated populations for irradiated products:

- Transplant patients (bone marrow or solid organ)
- Intrauterine transfusion , new born
- Cell-mediated immunodeficiences

DiGeorge, Wiskott-Aldrich, Leniier's disease, etc

- Hematologic malignancies & solid tumors treated with cytotoxic therapy.

PRC Infusion

- PRBCs issued for transfusion should be infused within 4 hours.
- Infusion rate of approximately 2.5 mL/kg/hour usually avoids circulatory overload
- Patients with cardiovascular instability may need to be transfused more slowly.

Platelets Components

PLATELETS

- Concentrate of platelets separated from a single unit of Whole Blood.
- One unit of Platelets contains 5.5×10^{10} platelets suspended in 40-70 mL of plasma.

POOLED PLATELETS

- Composed of individual platelet units combined by aseptic technique
- The number of units of Platelets in the pool will be indicated on the label.
- Usually 4 to 6units (4 to 6donors).

APHERESIS PLATELETS

- Effective way to harvest therapeutic adult doses of platelets from a single donor.
- Apheresis Platelets should contain $\geq 3.0 \times 10^{11}$ platelets.
- Plasma volume is indicated on the label and varies between 100 and 500 mL.

Patients with hypoproductive thrombocytopenia:

- Surgical bleeding does not occur until the platelet count is <50K

-Spontaneous bleeding in the absence of other risk factors does not usually occur until the platelet count is <10K

when to transfused

A platelet threshold of <10K can be used in patients without active bleeding.

- Dose is 0.2-0.4 u/kg or 10mL/kg per infusion to a maximum of 1 unit of Apheresis platelets
- platelets,Transfusion may proceed as quickly as tolerated - 10mL/kg/hour - Must take less than 4 hours.

FRESH FROZEN PLASMA

- 1 unit = 200 to 250ml
- Prepared from single units of whole blood.
- Frozen at -18 to -30oC.
- shelf life for 1 year
- Contains all of the coagulation factors and other proteins found in blood.

Factors are NOT concentrated

Indications FFP

- Patients who require replacement of multiple plasma coagulation factors (eg, liver disease, DIC).
- Patients undergoing massive transfusion who have clinically significant coagulation deficiencies.
- Patients taking warfarin who are bleeding or need to undergo to an invasive procedure before vitamin K could reverse wafering effect or who need only transient reversal of warfarin effect.
- Transfusion or plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP).
- Management of patients with selected coagulation factor deficiencies, for which no specific coagulation concentrates are available.

Contraindications FFP

- Do not use when coagulopathy can be corrected with specific therapy.

  - vitamin K , cryoprecipitate , coagulation factor concentrate

- Do not use when blood volume can be safely and adequately replaced with other volume expanders.
- Do not use as a source of albumin

Cryoprecipatate

- When FFP is thawed at4°C,a precipitate remains, which can be separated by centrifugation.
- Concentrated preparation that contains
  - Factor VIII (80-110 IU/bag)
  - fibrinogen (200 mg/bag) Factor XIII
    - von Willebrand factor (vWF) in fresh frozen plasma,
- Cryo is used in the treatment of deficiencies of fibrinogen and Factor XIII.
  - Congenital or Acquired Deficiencies

Cryoprecipatate

- First line therapy for control of bleeding associated with:
  -Fibrinogen deficiency
  - factoe XIII deficiency
- Second line therapy for:
  - von Willebrand disease
  - Factor VIII deficiency
- Do not use for DIC – does not contain all necessary factors (factor V)

CRYOPRECIPITATE DOSE

Hypofibrinogenemia:

- Number of bags = 0.2 × (weight)kg
  - ↑ fibrinogen approximately 50 to 100 mg/dL

Factor XIII deficiency:

- 1 bag/10kg

Bleeding in vWD

- 1 bag/10kg q 6-12 hours

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Ordering Blood Products like a Pro

Packed Red Blood Cells

- 10-20mLs/kg
- (ΔHb g/dL) x (weight kg) x 3.5 = volume (mLs) PRBCs

Platelet

- 10-20mls/kg
- Usual maximum is 1 apheresis unit

Fresh Frozen Plasm

- 10-15 ml/kg

Outline

- Donor & Recipient testing and compatibility
  - "Types", "Crosses" & "Screens"
- Blood Products
  - Where do they come from?
  - What are my option ?
- Ordering blood products like a professional
- Transfusion Complications
- Transfusion recommendations

Transfusion Associated Complications

Immunologic Complications

- **Immediate**
  - Acute hemolytic reactions
  - Febrile nonhemolytic reaction
  - Allergic/Anaphylactic reactions
  - Transfusion-related acute lung injury (TRALI)

-delayed

  - Delayed hemolytic reactions
  - Alloimmunization of antigens
  - Transfusion-associated graft-vs-host disease

Nonimmunologic Complications

- Transmission of infectious agents
  - virus, bacteria, parasites, and prions
- Transfusion associated circulatory overload(TACO)

Transfusion Associated Complications

If a transfusion reaction is suspected

1) STOP the transfusion and notify the blood bank immediately

2) Examine the patient

3) Send the following samples to blood bank for transfusion evaluation

- 1.5mL blood in clot blood tube
- 2.5mL blood in EDTA tube
- First post reaction urine specimen
- The blood product container and all attached fluids and recipient set.

• If the blood containers were discarded prior to the reaction, retrieve them if possible

Acute hemolytic reactions

- Immunologic destruction of transfused redcells
  - Usually the result of antigen incompatibility on donor cells with antibody in the recipient's circulation.
- Most common cause of severe,acute hemolytic transfusion reaction from ABO incompatible blood
- Signs and Symptoms
  - Common = rise (≥1◦C) in temperature from baseline and pulse with hemodynamic instability.
  - Possible = chills, dyspnea, chest/back pain, abnormal bleeding, or shock

Acute Hemolytic reaction

Laboratory findings

- Hemoglobinuria
- Elevation of serum bilirubin
- direct antiglobulin test (DAT) is usually positive

Treatment

-stop transfusion

- Measures to maintain blood pressure
- Correct coagulopathy (if present)
- Promote and maintain urine flow.

Lack of clinical symptoms does not exclude an acute hemolytic reaction.

Febrile Nonhemolytic Reactions

- Temperature elevation of ≥1◦C from baseline during or shortly after transfusion
  - absence of any other pyrexic stimulus.
- May reflect:
  - antibodies against donor white cells
  - action of cytokines
- Febrile reactions occur in ~1% of transfusion
  - more frequent:
    - Patients receiving non-leukocyte-reduced platelets
    - Previously alloimmunized by transfusion.
- Antipyretics usually provide effective symptomatic relief.
- Patients who experience repeated, severe febrile reactions may benefit from receiving leukocyte-reduced components

Allergic & Anaphylactic Reactions

Allergic reactions

- mild or self-limiting urticaria or wheezing that usually respond to antihistamines.
- No laboratory procedures are available to predict these reactions.

Anaphylactoid/Anaphylactic reactions

- characterizedby: hypotension,tachycardia,nausia/vomiting/diarhea abdominal pain,

dyspnea with pulmonary and/or laryngeal edema, bronchospasm and/or laryngospasm

- Rare but dangerous complications
  - Immediate treatment with epinephrine/steroids
- Reported in IgA-deficientpatients who develop IgA antibodies.

- Patients with a history of anaphylactic reactions might have less symptoms from washed cellular components

Transfusion-related acute lung injury (TRALI)

TRALI is defined as:
- Acute onset of hypoxemia with in 6 hours of a blood or blood component transfusion

Most common reported cause of transfusion-related deaths in the United States.

- Criteria for diagnosis
- Hypoximia
- Presence of bilateral infiltrates on frontal chest radiographs
- Exclusion of transfusion-associated circulatory overload(TACO),or preexisting acute lung injury.

- The exact mechanism of TRALI is not known
- Laboratory testing does not alter management of this reaction, which is diagnosed mainly on clinical and radiographic findings.
- Treatment of TRALI requires aggressive respiratory support, frequently requiring mechanical ventilation

Deleyed hemolytic reactions

- Occur in previously red cell-alloimmunized patients
  - Antigens on transfused red cells provoke anamnestic production of antibody.
- The antibody response reaches a significant circulating level while the transfused cells are still present in the circulation.
  - Usual time of presentation is 2 to 14 days after transfusion.
- Signs may include:
  - Fever (≥1 ◦C) above baseline, positive DAT, and unexplained decrease in hemoglobin/hematocrit with clinical signs of anemia.
  - Hemoglobinuria is uncommon, but ↑ LDH or bilirubin may be noted

Alloimmunization of Antigens

- **Alloimmunization to cellular antigens following transfusion RBCs , WBCs, platelets, orplasmaproteins**
- **Blood components contain certain immunizing substances other than those indicated on the label.**
  - **Example : platelet products may contain red cells and white cells.**
- **If a patient is challenged with an antigen that they previously have developed an antibody response too, then accelerated removal of cellular elements from the circulation and/or systemic symptoms are possible.**
- Clinically significant antibodies to red cell antigens will ordinarily be detected by pre-transfusion testing.
  - **Alloimmunization to antigens of white cells, platelets, or plasmaproteins can be detected only by specialized testing.**

Transfusion-associated graft-vs-host disease

- Rare but fatal
- Viable T lymphocytes in the transfused product engraft in the recipient and react against recipient tissue antigens.
- Follows transfusion with products that contains even very small numbers of viable T lymphocytes.
- Patients at risk include:
  - Transplant patients (bone marrow or solid organ)
  - Intrauterine transfusion
  - Cell-mediated immunodeficiences
    - DiGeorge, Wiskott-Aldrich, Leniier's disease, etc
  - Hematologic malignancies & solid tumors treated with cytotoxic therapy.
- Remains a risk with leukocyte-reduced components because they contain sufficient residual T lymphocytes.
- Irradiation of the component renders T lymphocytes incapable of proliferation and is presently the only approved means to prevent transfusion-associated graft-vs-host disease

Transfusion associated circulatory overload (TACO)

- TACO leading to pulmonary edema
  - Transfusion of excessive volumes
  - At excessively rapid rates.
- Risk in the very young and in patients with chronic severe anemia
- Small transfusion volumes can precipitate symptoms in at-risk patients who already have a positive fluid balance.
- Pulmonary edema should be promptly and aggressively treated.
- Infusion of colloid preparations should be reduced to a minimum
  - Including plasma components and the suspending plasma in cellular components.

transmission of Infectious Agents

Bacterial Contamination:

- Platelets then PRBCs are the most likely blood components to be contaminated with bacteria.
- Gram-positive skin flora are the most commonly recovered bacteria when prospective cultures of blood products are obtained.
- However, gram-negative organisms are most significant clinical entity.

• ≥50% fatality rate with transfusion associated gram-negative rod sepsis

• Symptoms during or immediately after transfusion.

- high fever(more than 2 c
- chills
- hypotension

•Symptoms associated with contamination by gram-positive organisms, may be delayed for several hours following transfusion.

•Emergent management:

- Contact blood bank immediately
- Broad-spectrum antibiotic therapy (gram positive and gram negative coverage)
- Cultures from the patient, suspected blood component(s), and administration set.
- Gram stain of suspected contaminated unit(s) should be performed whenever possible.