Blood Transfusion

Dr. Anas Albattikhi

General Surgeon

RATIONALE FOR TRANSFUSION

- Blood delivers oxygen to the tissues, and the vast majority of oxygen delivered is bound to hemoglobin in RBCs.

- The major physiologic considerations relevant to anemic patients are the degree to which oxygen delivery to the tissues is adequate and whether compensatory mechanisms for maintaining oxygen delivery will become overwhelmed or deleterious .
- (AFTER INCREASING tissue oxygen delivery by INCREASING CARDIAC OUTPUT over a range of hemoglobin concentrations)

Normal physiology

- Delivery of O_2 = cardiac output " STROKE VOLUME*HEART RATE" x arterial oxygen content
- At rest, there is a large reserve in oxygen delivery, since the rate of delivery normally exceeds consumption by a factor of four.
- Thus, if intravascular volume is maintained during bleeding and cardiovascular status is not impaired, oxygen delivery theoretically will be adequate until the hematocrit falls below 10 percent.

because :

greater cardiac output

rightward shift of the oxygen-hemoglobin dissociation curve

increased oxygen extraction

can compensate for the decrease in arterial oxygen content

Mechanisms that increase arterial oxygen content

Increased production of erythropoietin → hemoglobin synthesis
Rightward shift of oxyhemoglobin dissociation curve → increased O2 delivery

Mechanisms that increase cardiac output

Increased heart rate
Increased myocardial contractility
Decreased blood viscosity and decreased peripheral vascular resistance

- multicenter randomized controlled trials indicate that compared with a target hemoglobin of 10 g/dL, target hemoglobin values of 7 to 8 g/dL are associated with equivalent or better outcomes in most patient populations.

Impact of anemia on morbidity and mortality

- A retrospective database review of 310,311 veterans >65 years of age undergoing non-cardiac surgery evaluated the association of preoperative anemia with mortality or cardiac events .
- The adjusted odds of death or cardiac events correlated inversely with the preoperative hematocrit. Even mild anemia (HCT 36.0 to 38.9) was associated with a 10 percent increase in events; this rose to a 52 percent increased risk with more severe anemia (HCT 18.0 to 20.9).

  ……..

  An odds ratio (OR) is a measure of association between an exposure and an outcome , s an example, if the odds ratio is 1.5, the odds of disease after being exposed are 1.5 times greater than the odds of disease if you were not exposed

RISKS AND COMPLICATIONS OF TRANSFUSION

- Infection is a risk of transfusion since transfusion-transmitted pathogens. In addition, some studies have reported that transfusion-mediated immunosuppression may lead to increased risk of postoperative bacterial infection and anastomosis leak.
- Allergic and immune transfusion reactions.
- Volume overload is typically a concern in the elderly, small children.
- Hyperkalemia from potassium released from RBCs during blood bank storage.
- Iron overload .

Guidelines

AABB (formerly the American Association of Blood Banks), 2016 recommendations for hemodynamically stable patients without active bleeding

- Hemoglobin >10 g/dL – Transfusion generally not indicated except in exceptional circumstances.
- Hemoglobin 8 to 10 g/dL – Transfusion generally not indicated, but should be considered for some populations.
- Hemoglobin 7 to 8 g/dL – Transfusion may be appropriate in patients undergoing orthopedic surgery or cardiac surgery, and in those with stable cardiovascular disease.
- Hemoglobin 6 to 7 g/dL – Transfusion generally likely to be indicated.
- Hemoglobin <6 g/dL – Transfusion recommended except in exceptional circumstances.

Guidelines
AABB
American Association of Blood Banks

- Recommendation 1: a restrictive RBC transfusion threshold in which the transfusion is not indicated until the hemoglobin level is 7 g/dL is recommended for hospitalized adult patients who are hemodynamically stable, including critically ill patients, rather than when the hemoglobin level is 10 g/dL (strong recommendation, moderate quality evidence).
- A restrictive RBC transfusion threshold of 8 g/dL is recommended for patients undergoing orthopedic surgery, cardiac surgery, and those with preexisting cardiovascular disease (strong recommendation, moderate quality evidence).
- These recommendations do not apply to patients with acute coronary syndrome, severe thrombocytopenia (patients treated for hematological or oncological reasons who are at risk of bleeding), and chronic transfusion–dependent anemia (not recommended due to insufficient evidence).

Thresholds for red blood cell transfusion in adults

Condition	Hemoglobin threshold for transfusion
Symptomatic patient (eg, myocardial ischemia)	10 g/dL*[1,2]
Hospitalized patient	
Preexisting coronary artery disease	8 g/dL*[2]
Acute coronary syndromes	8 to 10 g/dL¶[2,3]
Intensive care unit (hemodynamically stable)	7 g/dL*[4,5]
Gastrointestinal bleeding (hemodynamically stable)	7 g/dL*[6]
Non-cardiac surgery	8 g/dL*[1]
Cardiac surgery	7.5 g/dL*[7,8]
Ambulatory outpatient	
Oncology patient in treatment	7 to 8 g/dL¶
Palliative care setting	As needed for symptoms; hospice benefits may vary

- There is excellent clinical trial evidence that suggests that a restrictive policy of transfusion at a hemoglobin concentration of 7 to 8 g/dL should guide transfusion decisions in most patients.
- The use of transfusion thresholds that restrict transfusion to this hemoglobin concentration are safe in most patient populations, may improve clinical outcomes, and will reduce unnecessary transfusion

- For most medical and surgical hospitalized hemodynamically stable patients, including those in the intensive care unit or with septic shock, it is recommended transfusion to maintain the hemoglobin at >7 g/dL rather than a higher threshold (Grade 1B EVEDINCE)
- however there may be cases in which the patient is asymptomatic at a hemoglobin of 7 g/dL, and clinician judgment may support not administering a transfusion.

Factors to consider

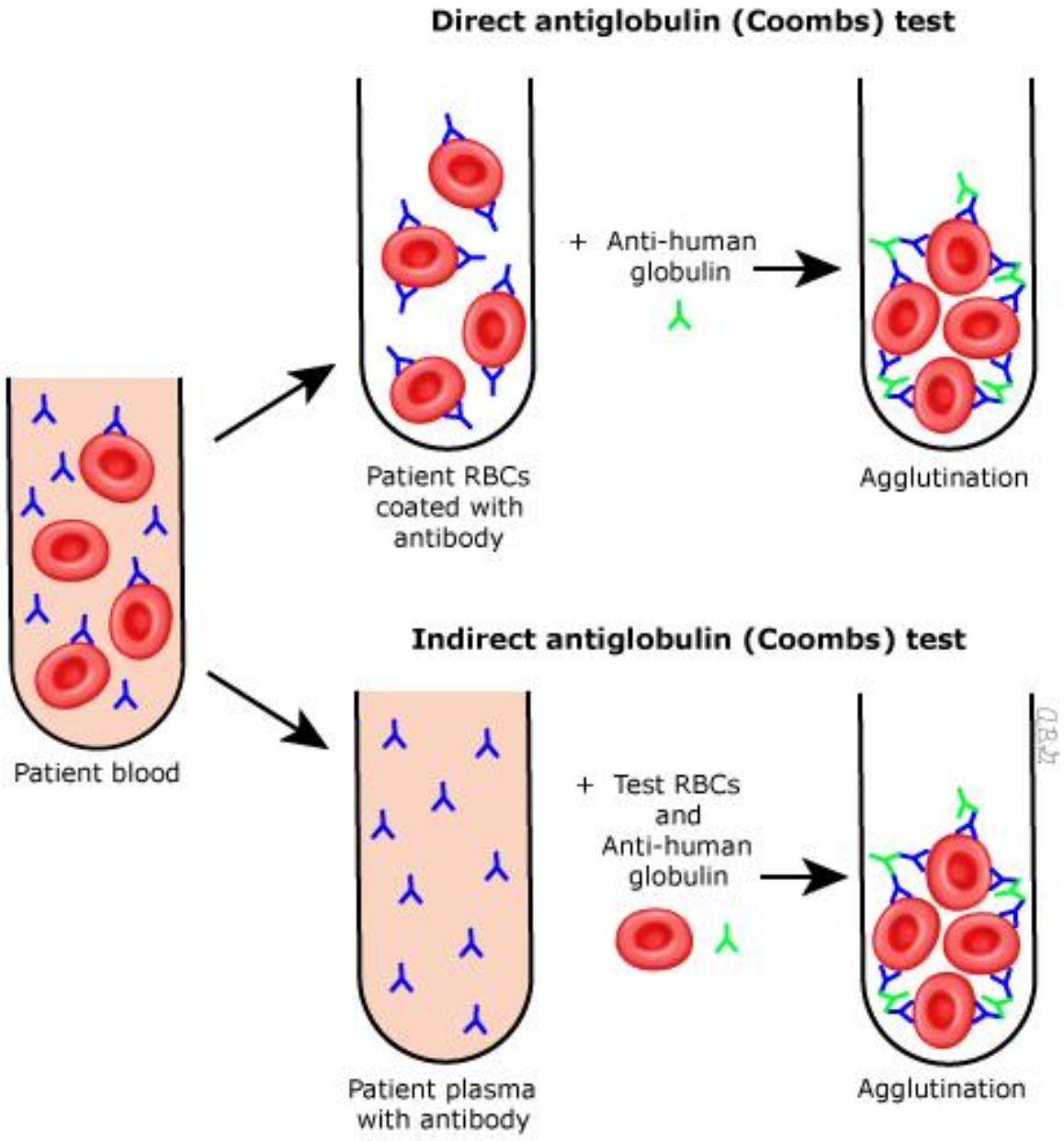
- The final decision to transfuse should incorporate the clinical status, co-morbidity, and the individual wishes of the patient.
- Assessment of the post-transfusion hemoglobin level can be performed as early as 15 minutes following transfusion, as long as the patient is not actively bleeding.

Major exceptions to the use of a threshold of 7 to 8 g/dL

- Symptomatic patients below 10 mmhg .
- Patients with acute coronary syndromes have not been adequately evaluated in clinical trials .
- Threshold-based transfusion is not appropriate for patients requiring massive transfusion.
- Severe thrombocytopenia in hematology/oncology patients at risk of bleeding.
- Chronic transfusion-dependent anemia.

PRE-TRANSFUSION TESTING

- **Antiglobulin (Coombs) testing**
- **Blood type** Blood type (also called blood group) refers to ABO and Rh(D) antigens expressed on an individual's RBCs
- **Crossmatch (compatibility testing)** – Crossmatch or compatibility testing refers to the selection and testing of a specific donor unit of RBCs for transfusion to the recipient.
- **Type and screen** – Type and screen refers to testing only on the recipient sample, including ABO and Rh(D) type and antibody screen


Direct antiglobulin (Coombs) test
+ Anti-human globulin
Patient RBCs coated with antibody
Agglutination
Patient blood
Indirect antiglobulin (Coombs) test
+ Test RBCs and Anti-human globulin
Patient plasma with antibody
Agglutination

SPECIMEN REQUIREMENTS
Specimen age/collection date

- there is no absolute requirement for the age/collection date of the sample in a patient who has not been exposed to foreign RBCs through recent transfusion or pregnancy.
- patients who have received a transfusion within the previous three months; or patients for whom the recent pregnancy and/or transfusion history is uncertain , samples for pretransfusion testing must be less than three days old.

Specimen collection tube

- In general, one 6 mL tube containing EDTA (eg, "pink top tube" or "purple top tube") is sufficient for all routine blood bank pre-transfusion testing, including type and screen and compatibility testing.
- Of note, hemolysis or lipemia may interfere with interpretation of agglutination due to color and/or cloudiness of the plasma.

Labeling

- labeling of the specimen must occur immediately after specimen collection.
- The person who draws the blood must identify the patient, preferably actively by asking the patient their name and date of birth, and label the date the blood was drawn.
- Information on the blood tube must match the information on the requisition for compatibility testing, and institution-specific specimen labeling policies should be followed.
- laboratories and transfusion services require two separate specimens for blood type verification in order to further reduce the chance of incorrect compatibility testing results based on a mislabeled specimen .

COLLECTION AND STORAGE PROCEDURES

- RBC are stored for up to 42 days
- for example citrate phosphate dextrose (CPD) for 21-day storage, CPD-adenine for 35-day storage, and the current generation of additive solutions that permit storage for 42 days.
- Regulations require that red cells be stored under refrigeration at controlled temperatures of 1 to 6°C to maintain the viability of the red cells and to prevent the growth of bacteria.

Freezing to preserve rare RBC units

- RBCs frozen in 40 percent glycerol are approved by the FDA and the AABB for storage at -80ºC for up to 10 years.
- The use of this product was evaluated in a prospective, randomized trial of 57 stable trauma patients who required blood transfusion . Compared with refrigerated RBC, frozen deglycerolized cells were noninferior with respect to increasing hematocrit, effects on thromboelastography parameters, and clinical outcomes.
- The need to subject red cells to glycerolization and freezing, and the time and effort required for thawing and washing immediately before infusion increases cost and delays transfusion. Thus, frozen deglycerolized red cells have a limited number of indications. These include the long-term storage of "rare" RBC units for transfusion of individuals with uncommon blood types

EFFECT OF STORAGE CONDITIONS ON TRANSFUSION OUTCOMES

- 2,3 BPG concentration
- Potassium leakage
- Citrate
- Ammonia
- Nitric oxide

PACKED RBCs VERSUS WHOLE BLOOD

- When citrate-phosphate-dextrose adenine (CPD-A1) is the anticoagulant used (35 day storage), the hematocrit of the RBC unit is approximately 65 to 80 percent, and the usual volume is between 225 and 350 mL.
- When an additive solution (AS) system is used (42 day storage), virtually all of the plasma is removed and then replaced with approximately 100 mL of storage solution resulting in a hematocrit of approximately 55 to 65 percent and a volume of 300 to 400 mL.
- Whole blood should be considered only when treating an adult who has bled acutely and massively.

Leukoreduced red cells

- HLA alloimmunization against class I antigens does not appear to occur if the red cell preparation contains less than 1 to 5 x 10^6 leukocytes.
- Some patients experience febrile transfusion reactions that are due to white cell contamination of the red cell concentrate rather than RBC alloimmunization.
- Leukoreduction is an effective method to prevent (or at a minimum, markedly reduce) the risk of transfusion-transmitted cytomegalovirus infection. CMV resides in the leukocytes and is removed during leukoreduction

Irradiated red cells

- In order to avoid the occurrence of graft-versus-host disease (GVHD) in patients who have immune deficiency states, transfused red cells must be subjected to irradiation with at least 25 Gy to prevent the donor T lymphocytes from dividing in the recipient.
- Irradiation to prevent “ GVHD “ is also recommended for red cells collected from relatives entered in directed donation programs

Washed red cells to remove plasma

- In order to prevent or eliminate complications associated with infusion of proteins present in the small amount of residual plasma in red cell concentrates, the unit of blood can be washed immediately before infusion. This approach is indicated for the following conditions:

●Patients with severe or recurrent allergic reactions (hives) associated with red cell transfusion.

●Certain patients with IgA deficiency when IgA deficient donors are not available (although frozen deglycerolized red cells may be the component of choice);

INFUSION PARAMETERS

- **Consent**
- **Premedication**
- **Filters** – All RBC units must be transfused through a standard 170 to 260 micron filter (contained as an integral part of a standard infusion set) designed to remove clots and aggregates.
- **Compatible fluids** – No other intravenous solutions or medications except 0.9 percent sodium chloride for injection, ABO compatible plasma, or albumin should be administered through the same tubing concurrently with the RBCs.

INFUSION PARAMETERS

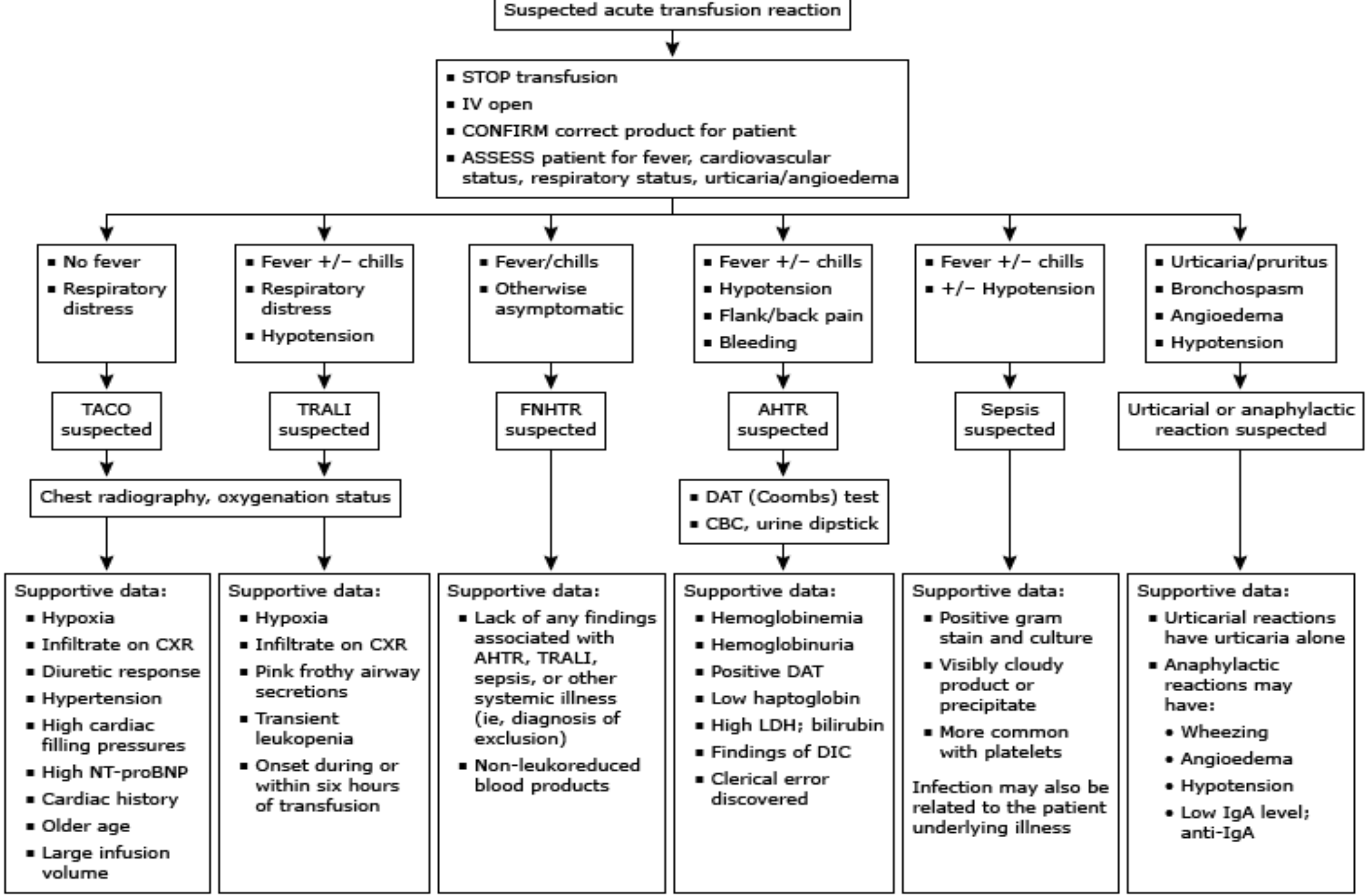
- **Infusion rate** – Suggested rates for adults are 1 to 2 mL per minute (60 to 120 mL per hour) for the first 15 minutes and then as rapidly as tolerated; the complete infusion should not exceed four hours.
- **Blood warmers** –blood warmers that raise the temperature closer to body temperature are used.
- **Post-transfusion hemoglobin level** – The post-transfusion hemoglobin level may be accurately measured as early as 15 minutes following transfusion.
- **Observation following transfusion** – In addition to observing the patient during transfusion, inpatients will continue to be observed for 15 to 30 minutes post-transfusion.

Transfusion Reaction

Reaction	Clinical findings	Laboratory findings	Implicated products and findings
Acute hemolytic reaction	Fever, chills, hypotension, back pain, DIC	Hemoglobinemia, hemoglobinuria, positive direct anti-globulin (Coombs) test (may be negative if all cell have hemolyzed), findings of DIC (prolonged PT, prolonged aPTT, low fibrinogen, thrombocytopenia)	RBCs, plasma (much less common), rarely platelets Intended recipient does not match actual recipient
Anaphylactic reaction	Hypotension, angioedema, wheezing, respiratory distress	Hypoxemia, IgA deficiency, anti-IgA	RBCs, platelets, plasma products
Acute lung injury (TRALI)	Respiratory distress, hypotension	Abnormal chest radiography, hypoxemia, transient leukopenia, anti-neutrophil or anti-HLA antibodies (if tested)	RBCs, platelets, plasma products
Circulatory overload (TACO)	Respiratory distress, rales	Abnormal chest radiography, hypoxemia, increased BNP or NT-proBNP	RBCs, platelets, plasma products
Sepsis/bacterial infection	Fever, chills, hypotension, DIC	Bacteremia, leukocytosis, findings of DIC	Platelets most commonly implicated, but can be any product Product may show bacterial contamination
Febrile non-hemolytic reaction	Fever	None	All blood products, but plasma is much rarer
Urticarial reaction	Hives	None unless specific	All blood products

- TACO is a form of circulatory volume overload that can occur in any individual and with transfusion of any blood component (eg, red blood cells [RBCs], platelets, plasma components such as Fresh Frozen Plasma [FFP], Cryoprecipitate). However, the volume transfused correlates with the risk of TACO, making TACO less likely with Cryoprecipitate than with FFP.
- Transfusion-related acute lung injury (TRALI) is a rare but potentially fatal complication of blood product transfusion. TRALI has been defined as new acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) occurring during or within six hours after blood product administration .

Feature	TRALI	TACO transfusion-associated circulatory overload
Body temperature	Fever may be present	Unchanged
Blood pressure	Hypotension may be present	Hypertension may be present
Respiratory symptoms	Acute dyspnea	Acute dyspnea
Neck veins	Unchanged	May be distended
Auscultation	Rales	Rales and S3 may be present
Chest radiograph	Diffuse bilateral infiltrates	Diffuse bilateral infiltrates
Ejection fraction	Normal	Decreased
PAOP	Most often 18 mmHg or less	Greater than 18 mmHg
Pulmonary edema fluid	Exudate	Transudate
Fluid balance	Neutral or negative	Positive
Response to diuretics	Inconsistent	Significant improvement
White cell count	Transient leukopenia may be present	Unchanged
BNP	<250 pg/mL	>1200 pg/mL


Suspected acute transfusion reaction
STOP transfusion
IV open
CONFIRM correct product for patient
ASSESS patient for fever, cardiovascular status, respiratory status, urticaria/angioedema
No fever
Respiratory distress
Fever +/− chills
Respiratory distress
Hypotension
Fever/chills
Otherwise asymptomatic
Fever +/− chills
Hypotension
Flank/back pain
Bleeding
Fever +/− chills
+/− Hypotension
Urticaria/pruritus
Bronchospasm
Angioedema
Hypotension
TACO suspected
TRALI suspected
FNHTR suspected
AHTR suspected
Sepsis suspected
Urticarial or anaphylactic reaction suspected
Chest radiography, oxygenation status
DAT (Coombs) test
CBC, urine dipstick
Supportive data:
Hypoxia
Infiltrate on CXR
Diuretic response
Hypertension
High cardiac filling pressures
High NT-proBNP
Cardiac history
Older age
Large infusion volume
Supportive data:
Hypoxia
Infiltrate on CXR
Pink frothy airway secretions
Transient leukopenia
Onset during or within six hours of transfusion
Supportive data:
Lack of any findings associated with AHTR, TRALI, sepsis, or other systemic illness (ie, diagnosis of exclusion)
Non-leukoreduced blood products
Supportive data:
Hemoglobinemia
Hemoglobinuria
Positive DAT
Low haptoglobin
High LDH; bilirubin
Findings of DIC
Clerical error discovered
Supportive data:
Positive gram stain and culture
Visibly cloudy product or precipitate
More common with platelets
Infection may also be related to the patient underlying illness
Supportive data:
Urticarial reactions have urticaria alone
Anaphylactic reactions may have:
Wheezing
Angioedema
Hypotension
Low IgA level; anti-IgA

FEBRILE NONHEMOLYTIC REACTIONS FNHTR

- the most common of all transfusion reactions.
- more frequent in children than adults.
- They are most likely with platelets prepared from platelet-rich plasma (ie, whole blood-derived platelets, as opposed to apheresis platelets), since these platelet products have the highest concentration of leukocytes.
- **Mechanism of FNHTR** — FNHTRs are commonly caused

* cytokines that are generated and accumulate during the storage of blood components.

* have been associated with antibodies directed against class I HLA antigens present on leukocytes in red cell concentrates.

* been associated with release of platelet-derived CD154 (CD40 ligand), which is capable of inducing production of proinflammatory cytokines

Clinical presentation and diagnosis of FNHTR

- occur within one to six hours after initiation of a transfusion; these include fever, often a chill, occasionally severe rigors.
- The temperature increase is typically in the range of 1 to 2°C. A temperature increase of <1°C is not considered clinically significant, while an increase of >2°C is more suggestive of an acute hemolytic or septic transfusion reaction.
- FNHTRs are diagnosed clinically by excluding other causes of fever in a patient receiving a transfusion .
- There is no laboratory or other testing that can confirm or exclude the presence of an FNHTR.
- The extent of the evaluation for other causes depends on the severity of the temperature increase and the presence or absence of other symptoms. As an example, a patient with fever, hypotension, and back pain should have a full evaluation for hemolytic transfusion reaction and possibly sepsis, whereas an individual with isolated mild fever may have a physical examination, clerical check of the transfusion, and visual inspection of the blood product.

Management of FNHTR

- Stopping of the transfusion.
- Administration of antipyretics if the fever is bothersome to the patient.
- Evaluation for other causes of fever, which include more serious (and potentially life-threatening) transfusion reactions as well as non-transfusion-related infection or fever.
- Administration of other medications, if needed, such as meperidine (25 to 50 mg) for severe chills or rigors.

Prevention of FNHTR

- pre-storage leukoreduction of the product (ie, removing most of the white blood cells by passing the cellular blood products through a filter shortly after the collection or using an apheresis collection technology with effective leukoreduction).
- Do **not** use premedications (eg, diphenhydramine, acetaminophen) to decrease the incidence of FNHTRs as they are ineffective and may cause adverse events on their own such as cardiovascular symptoms and central nervous system alterations.

Rapid overview: Emergency management of anaphylaxis in adults

Diagnosis is made clinically
The most common signs and symptoms are cutaneous (eg, sudden onset of generalized urticaria, angioedema, flushing, pruritus). However, 10 to 20% of patients have no skin findings.
Danger signs: Rapid progression of symptoms, respiratory distress (eg, stridor, wheezing, dyspnea, increased work of breathing, persistent cough, cyanosis), vomiting, abdominal pain, hypotension, dysrhythmia, chest pain, collapse.

Acute management

The first and most important treatment in anaphylaxis is epinephrine. There are NO absolute contraindications to epinephrine in the setting of anaphylaxis.
Airway: Immediate intubation if evidence of impending airway obstruction from angioedema. Delay may lead to complete obstruction. Intubation can be difficult and should be performed by the most experienced clinician available. Cricothyrotomy may be necessary.
Promptly and simultaneously, give:
IM epinephrine (1 mg/mL preparation): Give epinephrine 0.3 to 0.5 mg intramuscularly, preferably in the mid-outer thigh. Can repeat every 5 to 15 minutes (or more frequently), as needed. If epinephrine is injected promptly IM, most patients respond to one, two, or at most, three doses. If symptoms are not responding to epinephrine injections, prepare IV epinephrine for infusion (see below).
Place patient in recumbent position, if tolerated, and elevate lower extremities.
Oxygen: Give 8 to 10 L/minute via facemask or up to 100% oxygen, as needed.
Normal saline rapid bolus: Treat hypotension with rapid infusion of 1 to 2 liters IV. Repeat, as needed. Massive fluid shifts with severe loss of intravascular volume can occur.
Albuterol (salbutamol): For bronchospasm resistant to IM epinephrine, give 2.5 to 5 mg in 3 mL saline via nebulizer. Repeat, as needed.

Treatment of refractory symptoms:

Epinephrine infusion: For patients with inadequate response to IM epinephrine and IV saline, give epinephrine continuous infusion, beginning at **0.1 mcg/kg/minute** by infusion pump[Δ]. Titrate the dose continuously according to blood pressure, cardiac rate and function, and oxygenation.
Vasopressors: Some patients may require a second vasopressor (in addition to epinephrine). All vasopressors should be given by infusion pump, with the doses titrated continuously according to blood pressure and cardiac rate/function and oxygenation monitored by pulse oximetry.
Glucagon: Patients on beta-blockers may not respond to epinephrine and can be given glucagon 1 to 5 mg IV over 5 minutes, followed by infusion of 5 to 15 mcg/minute. Rapid administration of glucagon can cause vomiting.

ANAPHYLACTIC TRANSFUSION REACTIONS

- Rare but serious.
- Anaphylaxis results from sudden (typically massive) systemic release of mediators such as histamine and tryptase by mast cells and basophils, typically in response to an IgE-mediated (or IgG-mediated) immune reaction.

Clinical presentation and diagnosis of anaphylactic reactions

- Anaphylactic transfusion reactions are of rapid onset (as are all anaphylactic reactions), typically occurring within a few seconds to a few minutes following initiation of a transfusion. The patient may experience shock, hypotension, angioedema, respiratory distress, and/or wheezing.
- Diagnosis made clinically .

quantitative measuring of IgA levels as well as anti-IgA (if indicated), preferably on a pre-transfusion sample. Mast cell tryptase can be measured if the test is but the results generally do not alter diagnosis or management when the clinical diagnosis appears obvious.

Similarly, a chest radiograph could help distinguish between pulmonary edema and bronchospasm if these cannot be differentiated clinically.

URTICARIAL (ALLERGIC) REACTIONS

- Urticarial (allergic) reactions, characterized by hives without other allergic findings, are one of the most common transfusion reactions.
- urticarial transfusion reactions occur when a soluble substance in the plasma of the donated blood product (or the recipient) reacts with pre-existing IgE antibodies in the recipient (or the product)
- A commonly cited example of urticarial reactions is donor peanut allergy, with hives in the recipient triggered by recent peanut ingestion by the recipient.

Management and prevention of urticarial reactions

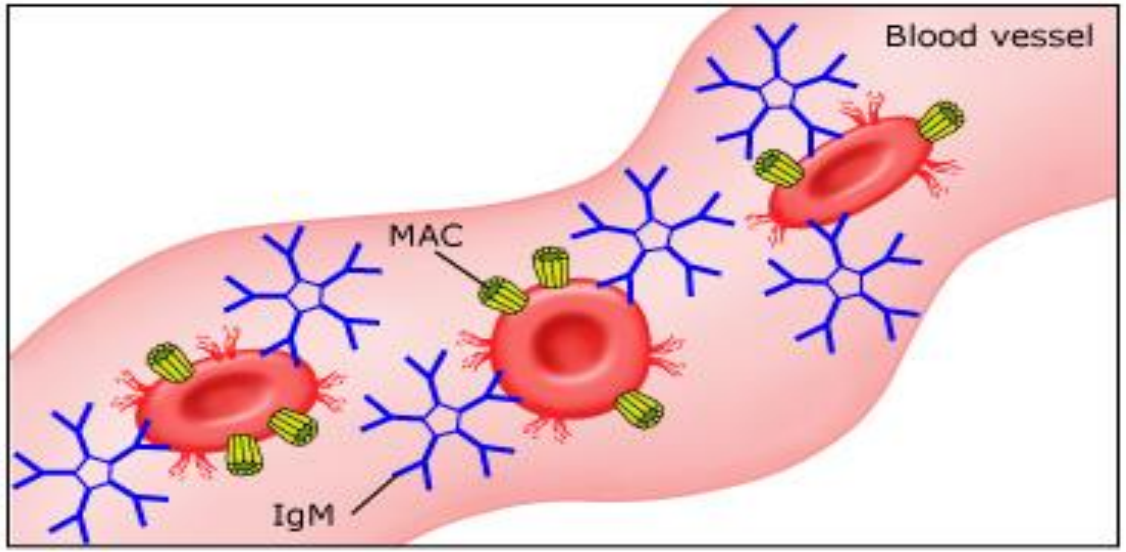
- the transfusion should first be stopped, and, if the urticaria is extensive, 25 to 50 mg of diphenhydramine can be given orally or intravenously. If the urticaria wanes and there is no evidence of dyspnea, hypotension, or anaphylaxis, the transfusion may be resumed.

HEMOLYTIC TRANSFUSION REACTIONS

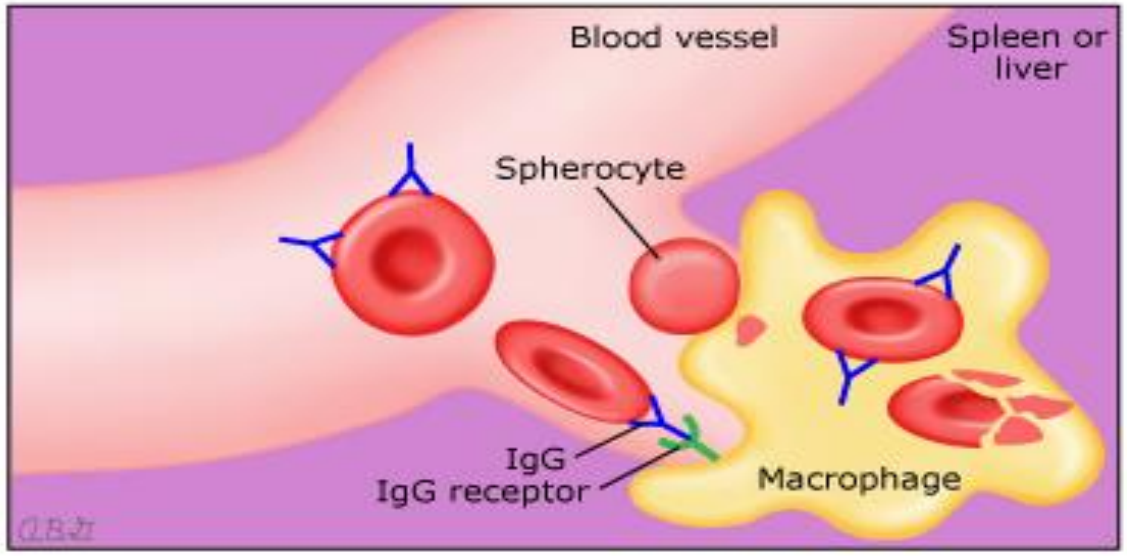
- Hemolytic transfusion reactions (HTRs) are characterized by immune-mediated red blood cell (RBC) destruction (hemolysis).

- They can be acute (during or within 24 hours after a transfusion) or delayed (days to weeks after a transfusion); and the hemolysis can be intravascular (releasing free hemoglobin into the circulation) or extravascular (resulting in removal of RBCs by the reticuloendothelial system)

A Intravascular hemolysis



B Extravascular hemolysis



AHTR

Acute HTRs (AHTRs) are hemolytic reactions

- occur during the transfusion or within 24 hours of completing the transfusion.
- AHTRs are typically associated with rapid intravascular hemolysis, which can lead to acute renal failure, disseminated intravascular coagulation (DIC), and hemodynamic collapse.
- the classic AHTR is a medical emergency requiring immediate intervention.
- Typical symptoms and findings include fever, chills, back or chest pain, and pink/red serum, plasma or urine, although the full "classic triad" of fever, flank pain, and red urine is rarely seen.
- In a patient under anesthesia or in a coma, evidence of DIC (oozing from intravenous catheter sites) may be the only finding.
- AHTRs are most commonly seen in the setting of ABO blood group incompatibility .

DHTR – Delayed HTRs (DHTRs) are hemolytic reaction

- occur more than 24 hours after completing the transfusion.
- Often, they occur days to weeks later.
- DHTRs are typically gradual and less severe; sometimes they are clinically silent.
- Laboratory findings may include a mild increase in anemia (or failure of the hemoglobin to increase as expected after transfusion) and evidence of extravascular hemolysis, which may include spherocytes on the peripheral blood smear.
- DHTRs almost always result from an anamnestic response following re-exposure to a foreign RBC antigen such as one from Rh system. Previous exposure may have occurred through transfusion or pregnancy.
- DHTRs generally do not require any treatment except for future avoidance of transfusions containing the implicated RBC antigen. If a DHTR is accompanied by more brisk hemolysis, more aggressive treatment may be required (ie, as for AHTR).

*anamnestic response. renewed rapid production of an antibody on the second (or subsequent) encounter with the same antigen

Management

- If the initial bedside evaluation (or subsequent testing) is consistent with intravascular hemolysis :

normal saline should be infused immediately to reduce the risks of hypotension and renal injury. An infusion rate of 100 to 200 mL/hour is typically used to support a urine output above 1 mL/kg/hour or 100 to 200 mL/hour to reduce the likelihood of acute oliguric renal failure .

The beneficial effect of urinary alkalinization in patients with marked hemoglobinuria is uncertain.

Vasopressors may be required to treat hypotension.

A nephrologist may be consulted for advice on prophylactic measures to prevent or reduce renal damage and in some cases to treat severe hyperkalemia

Management

- Repeat ABO compatibility testing.
- Additional antibody studies if ABO incompatibility is excluded.
- Repeat crossmatch .
- Direct antiglobulin (Coombs) testing (DAT), which may be positive in AHTR but may be negative in ABO incompatibility or if hemolysis is so severe that all RBCs with antibody on the surface have been lysed.
- Visual inspection of the serum and urine for pink or dark brown color. The serum should be analyzed for free hemoglobin, and a urine sample should be saved in case analysis of the urine for free hemoglobin is required. Pink or dark brown serum and/or urine and a positive test for free hemoglobin will be present in severe intravascular hemolysis but not in extravascular hemolysis.
- ●Testing for hemolysis with serum haptoglobin, lactate dehydrogenase (LDH), and unconjugated (indirect) bilirubin levels. In hemolysis, haptoglobin will be low; LDH and bilirubin will be increased, although the increase in unconjugated bilirubin may be delayed and is more likely to be helpful in evaluating the patient for a DHTR than for an AHTR.
- ●Testing for DIC if the patient has obvious signs of intravascular hemolysis (eg, pink serum or urine, hypotension) or signs of DIC such as oozing from intravenous sites or increased bleeding; DIC is a sign of severe intravascular hemolysis.
- ●Electrolyte testing and cardiac monitoring if the patient has obvious signs of intravascular hemolysis, since lysis of RBCs releases potassium into the circulation and may cause severe hyperkalemia.
- Serial hemoglobin levels,

Differential diagnosis of AHTR

- **Oxidative damage**
- **Immune hemolysis**
- **Autoimmune hemolytic anemia (AIHA) (** Warm agglutinins and drugs)
- **Direct red cell destruction**

Massive transfusion

- defined as the replacement by transfusion of 10 units of red cells in 24 hours, is a response to massive and uncontrolled hemorrhage.
- With more rapid and effective therapy, alternative definitions such as three units over one hour are more sensitive in identifying patients needing rapid issue of blood products for serious injuries because of uncontrolled hemorrhage.

- as volume is replaced, attention must be paid to coagulation parameters, platelet count, and metabolic status.
- preferably after each five units of blood replaced. If the PT and aPTT exceed 1.5 times the control value, the patient should be transfused with at least two units of fresh frozen plasma. If the platelet count falls below 50,000/microL, six units of random donor platelets, or one unit of apheresis platelets, should be given.
- Acid-base balance and the plasma ionized calcium and potassium levels should be periodically monitored, particularly in patients with coexistent liver or renal disease or in those with massive hemorrhage and low cardiac output.
- If 10 percent calcium gluconate is used, 10 to 20 mL should be given intravenously (into another vein) for each 500 mL of blood infused.

Platelet transfusion

- A unit of platelets isolated from a unit of donated blood contains approximately 7×10^{10} platelets, and four to six of these units are typically pooled for transfusion.
- Single donor (apheresis) platelets contain approximately 3 to 6×10^{11} platelets (ie, the equivalent of six or more units) per unit.
- Platelets are stored at room temperature; consequently their shelf life is only approximately five days
- Platelet transfusion can be lifesaving in bleeding patients with thrombocytopenia or reduced platelet function. Platelets should be transfused in any patient who is bleeding with a platelet count <50,000/microL (100,000/microL for central nervous system or ocular bleeding), or in any patient with an acquired or inherited platelet function defect regardless of platelet count

- It is use used as a prophylactic platelet transfusion to prevent spontaneous bleeding in most hospitalized afebrile patients with platelet counts below 10,000/microL due to bone marrow suppression.
- Patients with acute promyelocytic leukemia (APL) have a coexisting coagulopathy, and it is used a platelet transfusion threshold of 30,000 to 50,000/microL in these patients
- Platelets should not be used to treat thrombocytopenia due to platelet destruction such as ITP, TTP, HUS, HELLP syndrome, etc.

Dosage

- The volume of a dose of platelets is approximately 350-400mL. The initial recommended dose for an adult is 6 units of pooled random donor platelets or one apheresis unit; for pediatrics, the dose is 5-10mL/kg. This dose will usually increase the platelet count by approximately 25K-35K/microliter.

Plasma

- Fresh Frozen Plasma (FFP) – Plasma frozen within eight hours of collection
- •Plasma Frozen Within 24 Hours After Phlebotomy (PF24) – Plasma frozen within 24 hours of collection; also called Frozen Plasma
- •Thawed Plasma – Plasma that was frozen (ie, FFP or PF24), thawed, and kept at refrigerator temperature for up to five days

Plasma

- FFP, PF24, and Thawed Plasma are indicated for correction of major bleeding or in preparation for invasive procedures when the INR is substantially elevated.
- Plasma products should not be used as a source of albumin or nutrients, as a volume expander, or to correct a minimally elevated INR (ie, <2.0).
- Plasma generally is administered intravenously at a dose of 10 to 15 mL/kg of body weight..
- Due to the normal presence of A and/or B alloantibodies in patients with blood types A, B, and O, donor plasma must be either ABO-**identical** or ABO-**compatible** with the recipient.
- ●Risks of exposure to plasma include infection; volume overload (TACO); and febrile, allergic, anaphylactic, transfusion reactions, and transfusion-related acute lung injury (TRALI).

Cryoprecipitate

- Cryoprecipitate contains fibrinogen (factor I), factor VIII, fibronectin, factor XIII, and von Willebrand factor (VWF).
- ●Cryoprecipitate can be provided as single units or as "pools" containing five or more units.. In the average patient, each unit raises the plasma fibrinogen concentration by approximately 7 to 10 mg/dL; thus, 10 units will raise the fibrinogen by approximately 70 to 100 mg/dL in a 70 kg.
- cryoprecipitate carries risks of various types of transfusion reactions/complications.

Component (volume)	Contents	Indications and dose
Whole blood (1 unit = 500 mL)	RBCs, platelets, plasma	Rarely required. May be appropriate when massive bleeding requires transfusion of more than 5 to 7 units of RBCs (increasingly used in early trauma management).
RBCs in additive solution (1 unit = 350 mL)	RBCs	Anemia, bleeding. The increase in hemoglobin from 1 unit of RBCs will be approximately 1 g/dL; the increase in hematocrit will be approximately 3 percentage points.
FFP or other plasma product* (1 unit = 200 to 300 mL)	All soluble plasma proteins and clotting factors	Bleeding or expected bleeding (eg, emergency surgery) in individuals with deficiencies of multiple coagulation factors (eg, DIC, liver disease, massive transfusion, anticoagulation with warfarin or warfarin overdose if not corrected by vitamin K and/or PCC, depending on the clinical setting); therapeutic plasma exchange in TTP. FFP may be used to manage bleeding in individuals with isolated factor deficiencies (most often factor V) if a factor concentrate or recombinant factor is not available. In the rare event that FFP is used to replace a clotting factor, the dose is 10 to 20 mg/kg. This dose will raise the level of any factor, including fibrinogen, by close to 30%, which is typically sufficient for hemostasis.

Cryoprecipitate, also called "cryo" (1 unit = 10 to 20 mL)	Fibrinogen; factors VIII and XIII; VWF	Bleeding or expected bleeding with low fibrinogen: The increase in plasma fibrinogen from 1 unit of Cryoprecipitate per 10 kg body weight will be approximately 50 mg/dL. Bleeding or expected bleeding in individuals with deficiencies of factor XIII or factor VIII (hemophilia A) if a recombinant product or factor concentrate is unavailable. Bleeding or expected bleeding in individuals with VWD if DDAVP (desmopressin) is ineffective and recombinant VWF or a VWF concentrate is unavailable. Cryoprecipitate is generally provided in pools containing 5 units, and most patients receive one to two pools.
Platelets (derived from whole blood or apheresis) (1 unit of apheresis platelets or a 5 to 6 unit pool of platelets from whole blood = 200 to 300 mL)	Platelets	The platelet count increase from 5 to 6 units of whole blood-derived platelets or 1 unit of apheresis platelets will be approximately 30,000/microL in an average sized adult.