Blood Products & Transfusion

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Compatibility Testing

 Compatibility testing involves three separate procedures involving both donor and recipient blood.

 1. ABO & Rh blood type identification
 2. Antibody screening of donor plasma
 3. Donor/recipient crossmatch
ABO and Rhesus Typing

- Determine the ABO blood type and Rh status of both the donor and recipient.
- Most of the fatal hemolytic transfusion reactions result from the transfusion of ABO incompatible blood.
- Blood types are defined by the antigens present on the surface of the RBCs.
- Type A has A antigens on the surface of their red cells.
- Type B has B antigens
- Type AB has both A and B antigens
- Type O has neither antigen
The serum contains antibodies to the AB antigens that are lacking on the RBC.

- Type A has antibodies against the B antigen
- Type B has antibodies against the A antigen
- Type AB has no antibodies
- Type O has both anti-A and anti-B antibodies
Compatible Blood Types

- To determine which types are compatible you need to focus on which antibodies will be present in the recipient plasma. It is the reaction of the antibodies with donor RBC antigens that can activate the complement system and lead to intravascular hemolysis of the red cell.
- Type O- is the universal donor
- Type AB+ is the universal recipient
Rhesus (D) Antigen

- Patients with the Rhesus (D) antigen are said to be Rh+ and those without are Rh-.
- Anti-D antibodies are not constitutively present in the serum of an Rh-negative patient.
- 60-70% of Rh- patients exposed to Rh+ RBCs will develop anti-D antibodies.
- There is a latency period before the antibodies are synthesized.
### Blood types in the U.S. Population

<table>
<thead>
<tr>
<th>Group</th>
<th>Whites</th>
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<tbody>
<tr>
<td>O</td>
<td>45%</td>
<td>49%</td>
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<tr>
<td>A</td>
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<td>27%</td>
</tr>
<tr>
<td>B</td>
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<tr>
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<td>4%</td>
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<tr>
<td>Rh+</td>
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The Antibody Screen

- The antibody screen (which is an indirect Coombs test) is performed to identify recipient antibodies against RBC antigens.
- Commercially supplied RBCs which have been selected for certain antigens they possess, are mixed with both donor and recipient serum to screen for the presence of unexpected antibodies.
- If the recipient plasma screen is positive, the antibody will be identified and appropriate antigen negative donor units will be selected.
Antibody Screen

- If the patient has been transfused since the last antibody screening test, then the test should be repeated.
- Only 4 in 1,000 donations have unexpected antibodies.
- Estimated that only 1 in 10,000 screens will miss a potentially dangerous antibody.
- If the screen is negative only 1 in 50,000 units given will result in a hemolytic reaction.
The Crossmatch

- Donor RBCs are mixed with recipient serum.
- The test is performed in three phases and takes about 45 minutes.
- Phase 1  The Immediate Phase
- Phase 2  The Incubation Phase
- Phase 3  The Antiglobulin Phase
The Immediate Phase

- The Immediate phase serves primarily to ensure that there are no errors in the ABO typing.
- The test is performed by mixing donor RBCs and patient serum at room temperature for macroscopic agglutination.
- The test takes 1-5 minutes and detects ABO incompatibility and those antibodies in the MN, P, and Lewis systems.
The Incubation Phase

- This second phase involves incubation of the first phase reaction at 37°C in albumin and/or low-ionic strength salt solution.
- This aids the detection of incomplete antibodies that are able to attach to a specific antigen but are unable to cause agglutination in a saline solution.
- This phase takes 30-45 minutes to complete and primarily detects antibodies in the Rh system.
The Antiglobulin Phase

- This third phase of the crossmatch involves the addition of antiglobulin sera to the incubated test tubes.
- With this addition antibodies present in the sera become attached to the antibody globulin on the RBCs causing agglutination.
- This phase identifies the most incomplete antibodies from all blood groups systems including Rh, Kell, Kidd, and Duffy systems.
- This third phase is only performed on blood yielding a positive antibody screen and requires 60-90 minutes.
In previously transfused patients (or exposed during pregnancy), only 1 in 100 will have an antibody other than the anti-A, anti-B, and/or anti-Rh antibodies and many of these are non-reactive at physiologic temperatures.

Determining the ABO & Rh status alone yields a probability that the transfusion will be compatible in 99.8% of instances.

The addition of the antibody screen improves the compatibility to 99.94% and with a complete crossmatch to 99.95%.
Blood Products

- Whole Blood
- Red Blood Cells
- Platelets
- Fresh Frozen Plasma
- Cryoprecipitate
Red Blood Cells

- Whole blood is collected in bags containing citrate-phosphate-dextrose-adenine (CPDA) solution. The citrate chelates the calcium present in blood and prevents coagulation. The PRBCs are then prepared by centrifugation of the whole blood.

- CPDA blood has a Hct of 70-75% and contains 50-70 mL of residual plasma for a total volume of 250-275 mL and a shelf life of 35 days.
Additive Solution

- With the additive solution preparation the original preservative and most of the plasma is removed and replaced with 100 mL of Additive Solution.
- Lower Hct, 60%
- Less citrate per unit
- 75-80% fewer microaggregates
- Longer shelf life, 42 days
- Blood is able to regenerate 2,3-DPG more rapidly.
RBC Preparations

- Saline-washed RBCs may be used for patients that experience reactions to foreign proteins.

- White cells can be removed by washing, irradiation, or leukofiltration.
  - Irradiation is the only way to prevent GVHD post transplant
  - Leukoreduction makes PRBCs CMV safe

- One unit of RBCs will increase the Hb and Hct of a 70-kg adult by approximately 1g/dL and 3% respectively.
ASA Task Force Guidelines

- RBCs should usually be administered when the hemoglobin concentration is low (for example less than 6 g/dL in a young otherwise healthy patient) and the blood loss is acute, and transfusion is usually unnecessary when the hemoglobin is greater than 10 g/dL.

- The determination of whether intermediate levels of hemoglobin (between 6-10) justify or require RBCs should be based on any ongoing indication of organ ischemia, potential or ongoing bleeding, patient’s intravascular volume status and the patient’s risk factor for complications of inadequate oxygenation.
Fresh Frozen Plasma

- Plasma is separated from the RBC component of whole blood by centrifugation.
- One unit has a volume of 200-250 mL and contains all the plasma proteins, particularly factors V and VIII. It also contains the preservative added at the time of collection.
- FFP is frozen promptly to preserve two labile clotting factors (V and VIII) and thawed only immediately prior to administration.
- FFP must be ABO compatible but Rh+ plasma can be given to Rh- recipients, but should be avoided in young females because of the possibility of alloimmunization to the Rh antigen.
ASA Task Force Guidelines

- For urgent reversal of warfarin therapy (dose is 5-8 mL/kg of FFP)
- For correction of known coagulation factor deficiencies for which specific correlates are unavailable.
- For correction of microvascular bleeding in the presence of increased (>1.5 times normal) prothrombin time or partial thromboplastin time.
For correction of microvascular bleeding secondary to coagulation factor deficiency in patients transfused with more than one blood volume and when PT and aPTT cannot be obtained in a timely fashion.

FFP should be given in doses calculated to achieve a minimum of 30% of plasma factor concentration. (usually achieved with 10-15mL/kg of FFP)

FFP is contraindicated for augmentation of plasma volume or albumin concentration

For cases of antithrombin III deficiency

Treatment of immunodeficiencies

Treatment of thrombotic thrombocytopenia purpura
Platelets

- The platelets are separated from the plasma by centrifugation.
- Platelets are supplied either as single donor units or as a combination of multiple donors.
- One unit of platelets will increase the platelet count of a 70 kg adult by 5 to 10,000/mm³.
- Platelet viability is optimal at 22°C but storage is limited to 4-5 days.
- Platelets have both the ABO and HLA antigens. ABO compatibility is ideal but not required. (incompatibility will shorten the life span of the platelet)
ASA Task Force Recommendations

- Prophylactic platelet transfusion is ineffective and rarely indicated when thrombocytopenia is due to increased platelet destruction (e.g. ITP).
- Prophylactic platelet transfusion is rarely indicated in surgical patients with thrombocytopenia due to decreased platelet production when the platelet count is >100,000 and is usually indicated if the count is <50,000.
ASA Task Force Recommendations

- Vaginal deliveries or operative procedures ordinarily associated with insignificant blood loss may be undertaken in patients with platelet counts less than 50,000.

- Platelet transfusion may be indicated despite an apparently adequate platelet count if there is known platelet dysfunction and microvascular bleeding.
Cryoprecipitate

- Cryoprecipitate is the precipitate that remains when the FFP is thawed slowly at 4°C. It is a concentrated source of factor VIII, factor XIII, vWF, and fibrinogen.

- One unit of cryoprecipitate (which is the yield from one unit of FFP) contains sufficient fibrinogen to increase fibrinogen level 5 to 7 mg/dL. It usually comes in containers with 10 to 20 units.
Cryoprecipitate

- ABO compatibility is not essential because of the limited antibody content of the associated plasma vehicle (10 to 20 mL)
- Viruses can be transmitted with cryoprecipitate.
- It is stored at -20°C and thawed immediately prior to use.
- Cryoprecipitate is used in the treatment of factor VIII deficiency, hemophilia A and fibrinogen deficiencies.
Transfusion Risks

- Risks of blood transfusion can be divided into two categories
- Infectious
- Non-Infectious
Infectious Risks

- The transmittable risks are numerous and include:
  - Hepatitis A, B, C, D, E
  - Human T-cell lymphotropic viruses (HTLV-1 & HTLV-2)
  - HIV-1 & HIV-2
  - Cytomegalovirus
  - West Nile Virus
  - Epstein-Barr virus
Infectious Risks

- Parvovirus B19
- GBV-C virus (also called hepatitis G)
- Transfusion-transmitted virus (TTV)
- SEN virus
- Prions including Creutzfeldt-Jakob and variant
- Lyme Disease
- Bacterial infections including: malaria, Chagas disease, ehrlichiosis, babesiosis, and syphilis.
Transfusion Estimates

- Estimates of the frequency of infections are from North America and derived from the observed rates of seropositivity among donors and the statistical likelihood of administration of blood from donors whose infection is in the “window period” between contracting the virus and detectability by the available assays.

- With the recent advent of nucleic acid testing transmission rates are at very low levels.
Hepatitis B

- Rate of infection 1 in 350,000
- A NAT is now available and will most likely be implemented by 2008
- Estimated that only 35% of HBV exposed patients will develop acute disease
- 85% of patients the disease resolves spontaneously, 9% develop chronic persistent hepatitis, 3% develop chronic active hepatitis, 1% develop hepatocellular carcinoma.
Hepatitis C

- Rate of infection is 1 in 2,000,000
- HCV generally has a mild initial presentation, however, 85% of patients progress to a chronic state with significant associated morbidity and mortality.
- 20% of chronic carriers develop cirrhosis
- 1 to 5% develop hepatocellular carcinoma
Hepatitis A

- Rate of infection is very rare.
- Blood banks screen for HAV by history only and there is no carrier state for this virus.
- The infectious period is limited to 1 to 2 weeks
- The diagnosis depends on hepatitis antibody seroconversion.
Human Immunodeficiency Virus

- The most feared complication of any blood transfusion is the transmission of HIV
- The rate of transmission is 1 in 2,000,000
- HIV is a retrovirus, so called because its propagation requires translation of RNA to DNA
- The incidence has fallen dramatically since NAT testing.
- In the 1980’s rate of infection was 1 in 100. In 1997 the rate was 1 in 400,000.
Human T-Cell Lymphotropic Virus

- HTLV-1 and HTLV-2 belong to the same retrovirus family as HIV.
- The rate of infection is 1 in 2,900,000
- The incidence of clinical disease is very low.
- They are associated with T-cell leukemia and lymphoma rather than the generalized immunodeficiency of AIDS.
Cytomegalovirus

- Transfusion-associated CMV infections are usually benign and self-limited.
- CMV can cause serious, even fatal infections in the immunocompromised. Patients at risk include premature neonates, solid organ and bone marrow transplant recipients, and those with severely depressed immune function.
- Leukoreduction of RBCs reduces but does not prevent CMV transmission.
West Nile Virus

- WNV is a mosquito-borne flavivirus. It became epidemic in 2002 in the Midwestern states.
- The majority of infected individuals are either asymptomatic or develop only a mild illness, encephalitis or meningitis can occur.
- Death rate among confirmed cases is between 5-10%.
- Transmission by blood transfusion and organ transplantation has been confirmed.
West Nile Virus

- The window period between infection and clinical symptoms is short around 3 days.
- The period of infectivity also appears to be relatively brief also.
- NAT testing for WNV is being performed in areas of high incidence.
Parasitic Diseases

- Transfusion-transmitted malaria is relatively common in regions where the disease is endemic, but has been rare in the United States.
- The parasites reside within the red blood cell, so the hazard is almost exclusively with RBC transfusion.
- Chagas disease is caused by a protozoan and is endemic to South and Central America.
Prion-Related Diseases

- Prions are the causative agents of Creutzfeldt-Jakob disease (CJD) and variant Creutzfeldt-Jakob disease (vCJD).
- Both are fatal degenerative neurologic diseases caused by an abnormally folded variant of a protein that is constitutively present.
- The risk of transfusion related transmission is undefined.
- Only one case of transfusion related vCJD reported.
- The incubation period is up to 6 years, so the true rate may be under recognized.
- Between 1984 and 2004 156 cases of vCJD had been reported. All within the U.K. except for 10 cases.
Bacterial Contamination

- Bacterial Contamination occurs at a much higher frequency than any other infections and is associated with substantial mortality.

- Rate of bacterial infection/contamination:
  - RBCs 1 in 30,000
  - Platelets 1 in 2,000

The higher rate with platelets is because they are stored at room temperature and the units are generally pooled between 6 and 10 donor units.
Bacterial Contamination

- Fatalities are estimated to be between 1 in 1-6 million transfused units.
- The source of the bacteria can be donor blood, donor skin flora, or contaminants introduced during collection, processing, and storage.
- Numerous gram-positive and gram-negative organisms can occur. In order of frequency they are; Staphyloccus aureus, Klebsiella pneumoniae, Serratia marcescens, and Staphyloccus epidermidis.
Bacterial Contamination

- The patient who receives contaminated blood will rapidly experience some combination of fever, chills, tachycardia, emesis, and shock. The patient may also develop DIC and acute renal failure.

- If the index of suspicion is high then the blood transfusion should be stopped immediately and blood cultures taken.
Exposure Estimates

- Hepatitis B 1 in 350,000
- Hepatitis C 1 in 2,000,000
- HIV 1 in 2,000,000
- HTLV 1 in 2,900,000
- Bacterial reactions from
  - RBC 1 in 30,000
  - Platelets 1 in 2,000
Noninfectious Risks

- The noninfectious risks associated with blood products are generally immunologically mediated.
- Reactions can occur as a result of the antibodies that are constitutive (Anti-A or Anti-B) or ones that have been formed as a result of prior exposure to donor RBCs, WBC, platelets, or proteins.
Noninfectious Risks

- The noninfectious adverse reaction with their approximate incidences are:
  - Acute hemolytic transfusion reaction 1 in 25,000 to 50,000
  - Delayed hemolytic transfusion reaction 1 in 2,500
  - Minor allergic reactions 1 in 200 to 250
  - Anaphylactic/-toid reactions 1 in 25,000 to 50,000
  - Febrile reactions 1 in 200
  - Transfusion related acute lung injury 1 in 5,000
Acute Hemolytic Transfusion Reactions (AHTR)

- Hemolysis of donor RBC’s often leads to acute renal failure, DIC, and death.
- Of the >300 antigens on the RBC, only several will produce these reactions: anti-A, anti-B, anti-Kell, anti-Kidd, anti-Lewis, and anti-Duffy.
- ABO incompatibility is second only to TRALI of the three leading causes of transfusion related death.
When incompatible blood is given, antibodies and complement in the recipient plasma attack the antigens on the donor RBC.

Hemolysis ensues

The antigen-antibody complex activate the Hageman factor (factor XII), which acts on the kinin system to produce bradykinin.

Bradykinin increases capillary permeability and dilates arterioles, both which cause hypotension.
Activation of the complement system results in the release of histamine and serotonin from mast cells resulting in bronchospasm.

30% to 50% of patients develop DIC

Renal damage occurs for several reasons, blood flow is reduced because of hypotension and renal vasoconstriction, free hemoglobin can cause a mechanical obstruction, and if DIC occurs fibrin thrombi can be deposited in the renal vasculature
Signs and Symptoms of AHTR

- Fever
- Chills
- Nausea and Vomiting
- Diarrhea
- Rigors
- Hypotension
- Flushed appearance and dyspneic
- Chest pain and back pain
- Pt is restless, and has a headache
- Hemoglobinuria, and possible diffuse bleeding
Symptoms under GA

- Many signs and symptoms will be masked by general anesthesia.
- Hypotension, hemoglobinuria, and diffuse bleeding may be the only clues that a transfusion reaction has occurred.
- A reasonable index of suspicion should be maintained while administering blood products under GA.
Management of AHTR

- If a reaction is suspected, the transfusion should be stopped and the identity of the patient and the labeling of the blood rechecked.

- Management has 3 main objectives
  - Maintenance of systemic blood pressure
  - Preservation of renal function
  - Prevention of DIC
Management of AHTR

- Lab tests should include a repeat crossmatch and a direct antiglobulin (Coombs) test.
- The direct antiglobulin test is the definitive test for an acute hemolytic transfusion reaction.
- It examines recipient RBCs for the presence of surface immunoglobulins and complement. Patient serum is also examined for antibodies that react with donor cells.
Delayed Hemolytic Transfusion Reaction (DHTR)

- This reaction occurs when the donor RBCs have an antigen to which the recipient has been previously exposed by transfusion or pregnancy, however over time the antibodies fall to levels too low to be detected by compatibility testing.

- When re-exposure occurs the pt. undergoes an anamnestic response and produces more antibody that eventually lyses the foreign RBCs.
DHTR

- Evidence of hemolysis is usually evident by the first or second week after exposure.
- Symptoms are a low grade fever, increased bilirubin with or without jaundice, and a reduction in hemoglobin.
- Diagnosis confirmed by a Coombs test.
- The reaction is self-limiting and the clinical manifestations resolve as the transfused cells are removed.
Minor Allergic Reactions

- Allergic reactions to proteins in donor plasma can cause urticarial reactions in 0.5% of all transfusions.
- The reaction is almost always associated with FFP administration.
- The pt. may have itching, swelling, and a rash as a result of histamine release.
- Treatment is with diphenhydramine.
Anaphylactic Reactions

- This occurs in pts with hereditary IgA deficiency who have been sensitized by previous transfusions or pregnancy and are exposed to blood with foreign IgA protein.
- Reactions include dyspnea, bronchospasm, hypotension, laryngeal edema, chest pain, and shock.
- Treatment is with epinephrine and methylprednisolone.
Febrile Reactions

- Patients who receive multiple transfusions often develop antibodies to the HLA antigens on the passenger leukocytes.
- During subsequent RBC transfusions, febrile reactions may occur as a result of antibody attack on donor leukocytes.
- The response occurs in 1-2% of all RBCs transfused.
- Temperature increase of greater than 1 degree centigrade within 4 hours that resolves within 48 hrs.
Transfusion-Related Acute Lung Injury (TRALI)

- TRALI is a noncardiogenic form of pulmonary edema associated with blood product administration.
- It is associated with administration of all blood products but occurs most frequently with RBCs, FFP, and platelets.
- The incidence is 1 in 5000 units transfused.
- TRALI has a mortality of 5 to 8%.
- TRALI was the most common cause of transfusion related death from 2001-2003.
TRALI

- TRALI occurs when agents present in the plasma phase of donor blood activate leukocytes in the host.
- Those agents are usually antileukocyte antibodies in donor blood formed as a result of a previous transfusion or pregnancy.
- TRALI usually requires a preexisting condition such as sepsis, trauma, or surgery.
TRALI

- The clinical appearance is similar to adult respiratory distress syndrome (ARDS)
- Symptoms usually begin within 6 hours after the transfusion and often more rapidly, the patient develops dyspnea, cyanosis, chills, fever, hypotension and noncardiogenic pulmonary edema
- CXR reveals bilateral infiltrates
- Severe pulmonary insufficiency can develop
TRALI

- Treatment is largely supportive
- The transfusion should be stopped if the reaction is recognized in time
- The patient should receive oxygen and ventilatory support as necessary, usually with a low tidal volume strategy
Other Non-Infectious Risks

- Hypothermia
- Volume Overload
- Dilutional Coagulopathy
- Decrease in 2,3-DPG
- Acid-Base changes
- Hyperkalemia
- Citrate Intoxication
- Microaggregate Delivery