I. Title: Applications in Transfusion Medicine – A CBL Exercise

II. **Purpose:** At the conclusion of this exercise, students will be able to apply basic principles of transfusion medicine in health care settings, recognizing when and how blood products are utilized and what problems may arise in their usage. This exercise is primarily application along with explanatory basic pathophysiology. It is geared toward beginning students in health sciences, including medical, nursing, and physician's assistant students who would be working in clinical settings in which use of blood products may be encountered. They may work as a team to recognize, treat, and monitor patient care situations with use of blood products. Thus, this exercise may be appropriate as an interprofessional educational activity.

III. **Learning Objectives:** At the end of this exercise, the student will be able to:

1. Describe the indications for usage of the following blood products: packed red blood cells, platelets, fresh frozen plasma, and cryoprecipitate. Define "massive transfusion," and describe the metabolic derangements.
2. Describe and distinguish the following transfusion reactions: hemolytic, febrile, anaphylactic, circulatory overload, and transfusion-related acute lung injury (TRALI).
3. Define the infectious disease risks of blood products, including bacterial contamination, viral hepatitis B and C, HIV, HTLV, CMV, and malaria.
4. Define the meaning of and rationale for type and screen, and type and crossmatch, for blood products and explain the appropriate settings and processes for emergency release of blood and the use of "universal donor" blood.
5. Define alloimmunization in the context of hemolytic disease of the newborn. Describe the role of prenatal compatibility testing. Explain the role of Rh immune globulin prophylaxis in preventing hemolytic disease of the newborn.
6. Explain the clinical use of apheresis procedures, and give an example of how it is used.

IV. **Advance Preparation Assignment:** Basic information regarding transfusion medicine may be reviewed in the document:

Applications in Transfusion Medicine-Tutorial_Preparation.doc

This exercise is designed to be used in the basic science portion of the curriculum for health science students who have studied basic mechanisms of disease, including basic immunology, microbiology, and hematology.

V. Pre-test Questions:

There is pre-test with 6 questions that are at a more basic level to test preparation for the exercise, using the Advance Preparation Assignment. The constructs for these initial questions are then utilized in the 5 cases for discussion. The pre-test is comprised of the following questions:

1. A 30 year-old G2 P1 woman presents to the emergency department with third trimester vaginal bleeding and the sudden onset of marked pelvic pain. She is quickly admitted to labor and delivery, where severe fetal distress is discovered and ultrasound reveals placental abruption. An emergent cesarean section is performed, and packed red blood cells (PRBCs) are given, after which her hematocrit (Hct) is 25%. A few minutes after the male infant is delivered, her vaginal bleeding increases notably. Laboratory findings now reveal a prothrombin time (PT) of 90 seconds, partial thromboplastin time (PTT) 150 seconds, platelet count 15,000/mL, Hct 26%, fibrinogen 30 mg/dL, and D-Dimer 1:256. Which of the following therapies should the patient now receive?
    A. Cryoprecipitate and platelets
    B. O negative whole blood
    C. PRBCs only
    D. Plasmapheresis
    E. Single donor platelets

    Answer: A. Cryoprecipitate and platelets. This patient has DIC with a very low fibrinogen and platelet count, thus, she requires both cryoprecipitate and platelets, at the very least. The cryo has a high concentration of fibrinogen and other soluble coagulation factors, and the platelets will help with hemostasis. Although her hematocrit is low, she just received PRBCs and it appears to be improving. Whole blood may be used in some emergent situations, but it is not the best choice of therapy for this case. Lastly, her problems are not related to an antibody that could be removed with plasma exchange, thus ruling out plasmapheresis.

2. A 26 year-old man comes to the donor center as a volunteer donor for a directed donation to his mother-in-law, who is undergoing a left total hip arthroplasty. She is blood type O positive and CMV negative. Her preoperative Hct is 36.8%. Which of the following conditions will exclude using this young man's blood for use by this patient?
    A. His blood is CMV positive
    B. Her Hct is higher than 24%
    C. She may get transfusion associated graft versus host disease
    D. His blood type is A positive

Answer: D. His blood type is A positive. His blood type is incompatible with hers. On average, 50-80% of blood donors will be seropositive for CMV, and this blood is usable for the majority of situations requiring blood product therapy. While her preoperative hematocrit would certainly not indicate the transfusion of PRBCs, she may, however, experience bleeding during the surgery, indicating the need for it. He is also not directly related to the potential recipient, and as a result, there no increased risk for transfusion associated graft versus host disease.

3. A 40-year-old woman with severe thrombocytopenia is given a "six-pack" (6 units) platelet transfusion and a CBC drawn one hour later reveals an increase in the platelet count by 50,000/mL. Another CBC drawn 24 hours later reveals that the platelet count has only dropped by 5,000/mL. Three weeks later, the patient receives another six-pack platelet transfusion and this time the post-transfusion platelet count rises by 42,000/mL, and 24 hours later the count has now dropped by 35,000/mL. Her Hct has remained stable between 30 and 35% over this time. Which of the following conditions best explains these findings?
    A. Febrile transfusion reaction
    B. Disseminated Intravascular Coagulation (DIC)
    C. Alloimmunization
    D. Myelodysplastic syndrome
    E. Hypersplenism

    Answer: C. Alloimmunization. Using pooled platelets carries a risk for alloimmunization. Subsequent platelets transfused will be coated with antibody and quickly removed from circulation. If platelets must be given, the problem may be addressed with the use of more expensive HLA matched platelets from a single donor. Most febrile transfusion reactions are mild and platelets are not destroyed. DIC is a sentinel event with life-threatening ramifications, and her hematocrit would have dropped significantly due to microangiopathic hemolytic anemia associated with it. While cytopenias may occur with myelodysplasias, a differential drop in platelet count over time would not be expected. With hypersplenism, the initial platelet transfusion would have dropped more.

4. A 29 year-old primigravida has not had any prenatal care and shows up at the emergency room in labor with marked vaginal bleeding. An ultrasound scan shows placental abruption. Her Hct is now at 14% and she has orthostatic hypotension. In this situation, which blood product may be released for immediate transfusion without routine compatibility testing?
    A. Frozen, deglycerolized RBCs
    B. O negative PRBCs
    C. RBCs lacking high incidence antigens
    D. Irradiated blood
    E. AB negative whole blood

Answer: B. O negative PRBCs. This product may be released without compatibility testing (though is has already been processed by ABO and Rh typing), however, it is stressed that these units are only used in real emergencies as blood supplies are limited. Frozen units may be crossmatched, but they would require time for thawing and processing, thus not making them the best choice of therapy in an emergent situation as presented. While RBCs lacking high incidence antigens are useful to transfuse to individuals with alloantibodies to high incidence antigens, there is not enough time for a type and screen in this case. Irradiation would clear any leukocytes from the blood, but the blood would still have to be crossmatched. AB negative blood would pose serious risks for hemolysis if she had an incompatible blood type.

5. A 22 year-old male undergoes a right hemipelvectomy for treatment of metastatic rhabdomyosarcoma. He requires 10 units of PRBCs during the procedure. Following surgery, he is stable, with a Hct of 30%. A week later he develops a urinary tract infection from an indwelling catheter, which is complicated by acute pyelonephritis. A day later his blood pressure is 85/45 mm Hg. His peripheral blood smears shows schistocytes. He receives 5 units of FFP. As the 5th unit is being transfused, he develops sudden severe dyspnea and begins coughing up large quantities of frothy sputum. A chest radiograph shows bilateral pulmonary edema. He is most likely to have developed a transfusion reaction to which of the following blood components of blood?
    A. Albumin
    B. Fibrinogen
    C. Granulocytes
    D. Platelets
    E. Red blood cells

    Answer: C. Granulocytes. Transfusion related acute lung injury (TRALI) is caused when the donor plasma contains HLA or granulocyte specific antibodies which correspond to antigens found on the recipient patient's WBCs. Granulocyte enzymes are released, increasing capillary permeability and resulting in sudden pulmonary edema with respiratory distress. TRALI most often occurs with administration of blood products with plasma, such as FFP, and more often from donor women with more HLA antibodies from previous pregnancies. Transfusion reactions to albumin and fibrinogen do not occur. He did not receive any platelets, but platelet transfusion may cause alloimmunization and platelet destruction with subsequent transfusions. PRBCs may cause alloimmunization, and in more acute situations, hemolysis, but there are no signs of that in this case.

6. While driving to his next clinic visit, a 52 year-old man is involved in a vehicular accident in which his car is struck broadside at an intersection. Though the air bag

inflates, the car rolls over, and the impact against the door results in a large laceration to his left thigh. After transport to a local hospital, he is found to have a Hct of 16%. Coagulation studies reveal a PT of 16 seconds and a PTT of 26 seconds. His platelet count is 70,000/mL. Transfusion with which of the following blood products is most likely to be of benefit to this man?

A. Platelet packs
B. Packed red blood cells (PRBCs)
C. Fresh frozen plasma (FFP)
D. Cryoprecipitate (cryo)
E. Whole blood

Answer: B. PRBCs. The hematocrit is quite low, so he needs red cells. The most efficient, cost-efficient product is PRBCs. His coagulation studies do not suggest a need for coagulation factors or platelets. Although he is still actively bleeding, his platelet count is above 50,000/micoliter, thus not indicating platelet transfusion at this point. FFP would be useful to replace clotting factors, but his PTT is normal and his PT is only slightly prolonged. Cryo is not indicated in this case, and the use of whole blood would be a waste of resources.

Post-test Questions:

The 6 post-test questions are more challenging to answer and can be assigned for completion with group collaboration. If desired, the pre- and post-test questions can be completed as a whole at the end of the exercise, or included in any formal assessments in a course or block of teaching that includes this exercise.

1. A retrospective clinical study is performed to determine the risk associated with transfusion of blood products. The medical records of subjects who received transfusion therapy are reviewed. It is observed that a subset of subjects with one complication had a death rate near 100%. Which of the following complications from receiving blood products is most likely to have this death rate?
    A. Cytomegalovirus infection
    B. Allergic transfusion reaction
    C. Hepatitis B infection
    D. Graft versus host disease
    E. Febrile transfusion reaction

    Answer: D. Transfusion associated graft versus host disease. The GVHD encountered with transfusion is untreatable and nearly always fatal. Fortunately, it is rare. 50-80% of recipients are already CMV seropositive, and some immunocompromised hosts may benefit from receiving the antibodies to the virus. An allergic reaction may cause some hives and itching, but it would most likely not be life threatening. With extensive blood testing of donor blood, viral hepatitis transmission is not common. In cases that it does occur, recipients go on to chronic liver disease, which is not 100% fatal. A febrile transfusion reaction is generally not life threatening.

2. A 41 year-old woman has had headaches with blurred vision for 3 days. Over the past day she has developed increasing mental confusion with altered status. On admission to the hospital, she has vital signs showing a temperature of 37.9 C, P 104 bpm, RR 25/minute, and a BP of 70/40 mm Hg. She has petechial hemorrhages noted over her arms and trunk on physical examination, along with a stool sample positive for occult blood. Her CBC shows a hemoglobin of 9.1 g/dL, hematocrit (Hct) 27.7%, MCV 92 fL, RDW 19%, platelet count 8,900/mL, and WBC count 8,950/mL. Her peripheral blood smear shows schistocytes. A serum electrolyte panel shows sodium 147 mmol/L, potassium 5.0 mmol/L, chloride 105 mmol/L, CO_2 26 mmol/L, creatinine 2.9 mg/dL, urea nitrogen 32 mg/DL, and glucose 80 mg/dL. Which of the following therapies should she receive emergently?
    A. 6 pack of platelets
    B. 2 units of PRBCs
    C. Exploratory laparotomy
    D. Plasmapheresis
    E. Dopamine

    Answer: D. Plasmapheresis. Plasmapheresis with plasma exchange for fresh frozen plasma (FFP) is the treatment of choice for Thrombotic Thrombocytopenic

Purpura (TTP). The findings are consistent with TTP because of the pentad of neurologic abnormalities, fever, acute renal failure, microangiopathic hemolytic anemia, and thrombocytopenia. This condition is most often seen in adult women, and it can have an abrupt onset. Platelets are contraindicated as they will worsen the condition. Her Hct is not extremely low and thus PRBC transfusion is not indicated. She does not have the signs and symptoms requiring surgical intervention, and dopamine, while acting to raise her pressure, would not treat the underlying disease.

3. A 19 year-old female is a passenger involved in a motorcycle accident in which she incurs deep lacerations to her extremities. In the hospital she has an initial Hct of 22% and she begins to receive the first of 3 units of PRBCs. Within an hour her blood pressure drops precipitously. A peripheral blood smear reveals schistocytes. Her prothrombin time (PT) and partial thromboplastin time (PTT) are both prolonged. Her urine output drops, and what urine she does produce is red-brown. Which of the following complications of blood product therapy has most likely occurred?
    A. Anaphylactic transfusion reaction
    B. Hemolytic transfusion reaction
    C. Alloimmunization
    D. Febrile transfusion reaction
    E. Transfusion associated circulatory overload (TACO)

    Answer: B. Hemolytic transfusion reaction. ABO incompatibilities are rare but can occur if the wrong blood is given due to clerical errors. Even in emergent situation is it important to take time to properly label specimens and to properly identify patients. Allergic transfusion reactions are usually in response to transfused plasma proteins and results in itching and hives. Alloimmunization typically results in platelet destruction, not RBC destruction. Febrile reactions would not result in hemolysis. TACO would result in pulmonary edema.

4. A laboratory study is performed to determine what screening procedures need to be performed to help prevent transfusion-acquired infections. Laboratory testing is performed on potential donors. It is observed that antibodies to one infectious agent are found in 60 to 100% of the adult population in the U.S. It is determined that no routine blood screening will be performed for this agent. Which of the following organisms is most likely to fit this criterion?
    A. Hepatitis A virus
    B. HTLV-1
    C. Cytomegalovirus
    D. Malaria
    E. Hepatitis C virus

    Answer: C. Cytomegalovirus. Nearly everyone has been exposed to CMV and has some antibody. Finding CMV negative units is difficult. Hepatitis A virus is not tested for, but the incidence of disease in the U.S. is not this high. Blood

banks currently test for HTLV-1 and Hepatitis C, while a travel history aids in screening for malaria, as it's not easily tested. Anyone visiting an area where malaria is endemic is excluded as a donor for six months.

5. A laboratory study is conducted to determine whether cryoprecipitate or fresh frozen plasma (FFP) is of greater use in treating different coagulopathies. A deficiency involving which of the following coagulation factors is most likely to be found to require FFP therapy?
    A. Fibrinogen
    B. Prothrombin
    C. von Willebrand factor
    D. Factor VIII
    E. Factor XIII

    Answer: B. Prothrombin. FFP is the component that contains all of the soluble coagulation factors. Fibrinogen is present in cryoprecipitate, and it is useful in the treatment of hypofibrinogenemia due to DIC. vWF, Factor VIII and Factor XIII are all also in cryo.

6. A 24 year-old G4 P2 woman gives birth at 35 weeks gestation to twin female infants. Both infants are noted to have marked fetal hydrops along with generalized icterus. The infants' peripheral blood smears demonstrate numerous nucleated RBCs, and the spun Hct is only 20%. Which of the following mechanisms is most likely to produce these infants' disease?

    A. Twin-twin transfusion syndrome
    B. Naturally occurring maternal antibodies
    C. Fetal autoantibody production
    D. Prior maternal sensitization to fetal antigens
    E. Congenital HIV infection

    Answer: D. Maternal sensitization to fetal serum antigens from previous pregnancies. Hemolytic disease of the newborn (HMD) is a cause for fetal hydrops. This is usually the result of maternal sensitization from a previous pregnancy. The mother is typically Rh negative and the baby Rh positive. The majority of cases of HMD are due to Rh incompatibility. A monochorionic placenta can have a vascular anastomosis which allows blood to flow from one fetal circulation to the other, however, hemolysis does not occur. Naturally occurring anti-A and anti-B antibodies are typically IgM and do not cross the placenta, and autoimmune mechanisms of disease are unlikely in fetal life. HIV infection does not produce hemolytic disease of the newborn.

The discussion at the end of the exercise regarding the questions can cover both the pre-test and the post-test.

VI. Group Cases for Discussion:

Case 1: Blood Products and Massive Transfusion

History: F.R. is a 17 year-old Caucasian male who is brought into the Trauma wing of the Emergency Department by EMS following a motor vehicle accident. F.R. is unresponsive and cyanotic, around his lips, but he does have carotid and femoral pulses.

Physical Examination: Vital signs are P 115 bpm, BP 80/40 mm Hg, T 37.6 C, and RR 24. Physical examination finds large lacerations and scrapes throughout, a compound fracture of his right femur, and a digital rectal exam that is positive for occult blood. Bruising and petechiae are also noted, mostly around the fracture site. PERRLA and Neuromuscular exam is intact.

Laboratory Data:	Patient	Normal Ranges
Hemoglobin	5 g/dl	(14.6 – 17.8 g/dL)
Hematocrit	15%	(40.8 – 51.9%)
Platelet count	35	(177 – 408 K/mL)
Prothrombin time (PT)	30 seconds	12-15.5 seconds
INR	2.4	
Partial thromboplastin time	50 seconds	24 – 35 seconds
Fibrinogen	30	(150 – 430 mg/dL)
D-Dimer	5	(0 – 0.4 microgram/mL)

The peripheral blood smears show schistocytes.

Course: Multiple large bore IV access lines are established, and 6 units of PRBCs are infused with 0.9% normal saline. He also receives platelets and FFP.

Case 1 Questions:

Q1.1 What is the assessment for F.R, and how will his case be followed and managed from this point forward?

Answer: F.R. has gone into Disseminated Intravascular Coagulation (DIC), a life threatening condition, s/p a major traumatic incident. DIC is a consumptive coagulopathy that results in the excessive activation of platelets and clotting factors, leading to the formation of mass blood clots. In the process, platelets and clotting factors are consumed, resulting in low platelet counts, prolonged PT/INR/PTT, and low

fibrinogen. Also, plasminogen is activated to break down the thrombi, resulting in the markedly elevated D-Dimer, a test for the fibrin degradation products.

DIC is a form of microangiopathic hemolytic anemia (MAHA), with the formation of schistocytes, which can be seen in the peripheral blood smear. Although the traumatic event is mostly responsible for the massive blood loss and decreased hemoglobin and hematocrit, the MAHA also contributes.

With the transfusion of blood products, his disease will be managed with the close monitoring of his hemoglobin, hematocrit, platelet count, PT/INR/PTT, and D-Dimer. Depending on his response to treatment and the changes in these values, the transfusion of additional blood products may be indicated.

Q1.2 What are indications for and potential complications of massive PRBC transfusion?

Answer: The usage of packed red blood cells (PRBCs) is generally indicated with a hemoglobin of 7-8 g/dL in hospitalized stable patients. Transfusion is considered when there is a markedly decreased O_2 saturation. The presence of orthostatic hypotension may indicate volume loss, including blood loss. the presence of organ dysfunction should be considered before utilizing blood products. In this case, there was massive blood loss, which s defined as the loss of one blood volume within a 24 hour period, a 50% loss in less than 3 hours for acute scenarios, or a rate of loss of 150 ml/min.

Acute anemia from major blood loss may indicate the need for massive transfusion (MT). Massive transfusion is the lifesaving treatment of hemorrhagic shock that requires the transfusion of one blood volume. Major complications that may arise in patients who require massive transfusion include hypothermia, coagulopathy, and/or electrolyte abnormalities and metabolic derangements, such as acidosis and alkalosis.

The efficacy of transfusion of PRBCs is typically measured with the hemoglobin and hematocrit with careful monitoring of the patient's vital signs for adverse reactions.

Q1.3 What are the indications for and potential complications of platelet transfusion?

Answer: In this case, the usage of platelets is indicated with a platelet count of less than 50,000 and there is active bleeding. The efficacy of treatment is measured by post-transfusion platelet count. If the count drops quickly, it is likely that platelets are being consumed rapidly and further transfusions of platelets may be ineffective.

Bacterial contamination is infrequent but more likely to occur with the transfusion of platelets because of their storage at room temperature, than other blood products that are refrigerated.

Q1.4 What are the indications for FFP?

Answer: FFP is indicated when a patient has MULTIPLE factor deficiencies and is BLEEDING, or for TTP. The PT and PTT will be prolonged, and the INR generally should be greater than 1.6. The efficacy of FFP can be monitored with coagulation testing.

Case 1 Discussion:

Learning Objectives

1. Disseminated Intravascular Coagulation
2. Massive blood loss and transfusion
3. Blood products

D1.1 Disseminated Intravascular Coagulation (DIC)

DIC, a life threatening condition, is a consumptive coagulopathy that results in the excessive activation of platelets and clotting factors, leading to the formation of widespread fibrin thrombi in the microcirculation. In the process, platelets and clotting factors are consumed, resulting in low platelet counts, prolonged PT/INR/PTT, and low fibrinogen. Simultaneously, the fibrinolytic pathway is activated with plasminogen being converted to plasmin to actively break down the fibrin clots. This is reflected in a markedly elevated D-Dimer, a test for the fibrin degradation products. As a result, a hyperactive clotting disorder results in mass hemorrhaging.

DIC is a form of microangiopathic hemolytic anemia (MAHA), with the formation of schistocytes, which can be seen in the peripheral blood smear.

DIC is not a primary disease, but instead results as a complication of an underlying disease. Treating DIC involves treating the underlying cause and managing the symptoms.

D1.2 Massive blood less and transfusion

Major blood loss is defined as the loss of one blood volume within a 24 hour period, a 50% loss in less than 3 hours for acute scenarios, or a rate of loss of 150 ml/min. Acute anemia from major blood loss may indicate the need for massive transfusion (MT). **Massive transfusion** is the lifesaving treatment of hemorrhagic shock that requires the transfusion of one blood volume. Major complications that may arise in patients who require massive transfusion include hypothermia, coagulopathy and/or electrolyte abnormalities and metabolic derangements, such as acidosis and alkalosis.

Hypothermia

Hypothermia in patients with MT occurs as a result of

- Exposure
- Infusion of cold fluids and blood products
- Opening of body cavities
- Decreased heat production
- Impaired thermoregulatory control

Hypothermia may lead to decreased metabolic, drug and hepatic metabolism with diminished immune responses and clot formation. It may be avoided by elevating the room temperature, warming the patient with heating blankets and the use of blood warmers during infusion.

Coagulopathy

Hemostatic abnormalities may arise in patients requiring MT due to a combination of dilution, consumption of clotting factors and fibrinolysis. Coupled with hypothermia, impaired clot formation may further exacerbate blood loss. Coagulation is monitored with laboratory testing of the PT, PTT, and INR, and it may be avoided by transfusing PRBC:FFP:platelets in a 1:1:1 ratio or the use of recombinant factor VIIa as indicated.

Electrolyte abnormalities and metabolic derangements

Serum potassium, calcium and magnesium may be disregulated with MT. As a result, cardiac arrest due to hyperkalemia; tetany, decreased myocardial contractility and hypotension due to hypocalcemia; and prolonged QT interval with hypomagnesemia are potential serious complications. I**t is critical that the healthcare provider closely monitor Potassium, Calcium and Magnesium levels before and after transfusion, and corrections must be done as indicated.**

Alkalosis and Acidosis

Blood is typically stored in citrate phosphate dextrose adenine (CPAD) solutions with a pH of 7.0 for most fresh PRBC units. As blood ages, citrate is metabolized to bicarbonate, and in patients who require MT, metabolic alkalosis may occur. Metabolic acidosis arises a result of the hypoperfusion of tissues and is not directly related to blood product administration. The acidosis may be temporarily managed with the use of alkalinizing agents such as sodium bicarbonate or tromethamine, such as the case of patients with metabolic acidosis due to renal dysfunction or impairment. In acute patients, however, aggressive resuscitative efforts should be continued as the restoration of adequate tissue perfusion is paramount to the reversal of the underlying acidosis.

Complications from acidosis include coagulopathy and impaired hemostasis due to the inhibition of clotting factors and clot formation.

D1.3 Blood Products

There are a variety of blood products, pharmacologic agents, and procedures that can be utilized to treat anemia, thrombocytopenia, and bleeding disorders. Here is a brief overview of the products and services available:

Packed Red Blood Cells (PRBCs)

Packed red blood cells (PRBCs) are made from a unit of whole blood by centrifugation

and removal of most of the plasma, leaving a unit with a hematocrit of about 60%. **One PRBC unit will raise the hemoglobin 1 g/dl and the hematocrit of a standard adult patient by 3%** (or about 1%/mL/kg in a child - 12%/25 kg with the standard 300 mL PRBC unit).

PRBCs are used to replace red cell mass when tissue oxygenation is impaired by acute or chronic anemia. The usage of PRBCs are generally indicated with a hemoglobin of 7-8 g/dl, a markedly decreased O2 saturation, and/or orthostatic hypotension.
Infusion should proceed at the fastest rate the patient can tolerate, but less than 4 hours. The efficacy and effects of transfusion of PRBCs are monitored via physical findings and laboratory testing. Vital signs are typically logged in 15 minute intervals, and hemoglobin and hematocrit levels are determined as a part of the Complete Blood Count (CBC).
PRBCs can be further specialized depending on the indication, such as if agents need to be reduced or removed from the unit. These include:

- **Washed Red Blood Cells**: A unit of packed red blood cells (PRBCs) is washed to reduce plasma proteins. This reduces the risk for allergic transfusion reactions. Washing reduces immunoglobulins, such as anti-IgA that could cause anaphylactic transfusion reactions in persons with selective IgA deficiency.

- **Leukocyte Reduced**: Red blood cell and platelet units may be filtered to remove most of the leukocytes (white blood cells). This may reduce the risk for febrile transfusion reactions, may help prevent alloimmunization to MHC (HLA) donor antigens, and help reduce the risk for cytomegalovirus (CMV) infection.

- **Irradiated Blood**: Irradiation is needed to destroy all nucleated cells and living leukocytes (white blood cells), particularly lymphocytes that could cause transfusion associated graft versus host disease (TAGVD).

Fresh Frozen Plasma (FFP)

FFP contains all factors of the soluble coagulation system, including factors II, V, VII, IX, X and XI. FFP is indicated when a patient has MULTIPLE factor deficiencies and is BLEEDING, or for TTP. The PT and PTT will be prolonged, and the INR generally should be greater than 1.6. **Note that FFP SHOULD NEVER be used as a plasma expander.**

The efficacy of FFP can be monitored with coagulation testing.

Cryoprecipitate

Cryoprecipitate (cryo) contains a concentrated subset of FFP components including fibrinogen, factor VIII coagulant, vonWillebrand factor, and factor XIII. Cryoprecipitate is

used for hypofibrinogenemia, von Willebrand disease, and in situations calling for a "fibrin glue." Cryo IS NOT just a concentrate of FFP. In fact, a unit of cryo contains only 40-50% of the coag factors found in a unit of FFP, but those factors are more concentrated in the cryo (less volume).

Platelets

A single platelet unit is derived from one whole blood unit collected. Platelets are stored at room temperature and CANNOT be frozen. They must be used in 5 days. Pooled platelets from multiple donors from whole blood collections are cheaper to produce but the exposure to the recipient increases.

A "six pack" of platelets can be obtained by apheresis from a single donor at one time. Thus, apheresis platelets give just "one donor" exposure to the recipient, but the cost is high. The recipient's HLA type can be "matched" to a platelet donor with a similar HLA type to deal with problems of HLA alloimmunization (in patients with prior transfusions or pregnancies). The expected incremental increase in platelet count for adults is 30 - 60 K for each "six pack" of platelets.

The usage of platelets is indicated if the platelet count (in microliters) is

- Less than 10,000 in a stable patient;
- Less than 50,000 and there is active bleeding;
- Less than 50,000 and an invasive or surgical procedures is planned;
- Less than 100,000 and a neurosurgical procedure is planned
-

Upon administration of platelets, the efficacy of treatment is measured by post-transfusion platelet count. If the count drops quickly, it is likely that platelets are being consumed rapidly and further transfusions of platelets may be ineffective.

Non-Blood Components Available for Transfusion

Normal Saline

Normal saline is used when providing vascular access and fluid volume when transfusing other products and pharmacologic agents. Normal saline is more readily accessible than albumin or FFP, it is relatively inexpensive, and it does not have the risk of viral transmission.

Albumin

Albumin is useful as a plasma expander. Albumin is not always readily accessible and it is expensive, but it does not have the risk of viral transmission.

Case 1: References

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Case 2: Transfusion Reactions

History: D.L. is a 65 year-old African-American female with osteoarthritis of the right hip. She has no other major medical problems. She has 4 living children who are healthy. She has no known drug allergies. She is taking no medications other than acetaminophen for her constant pain.

She is scheduled for a right total hip arthroplasty. A preoperative workup shows a normal prothrombin time, partial thromboplastin time, white blood cell count, and platelet count. Her hemoglobin is 12 g/dL and hematocrit 36%. A blood type and screen is obtained and she is O positive with antibody screen negative.

During the operation she begins to bleed. An order for 4 units of PRBCs is sent, and since no crossmatched units are on reserve, a release is given for type specific blood. She receives 4 units of PRBCs intra-operatively. She stabilizes and the surgery proceeds without any further complications.

Course: Over the next 4 hours while recovering in the PACU, she develops respiratory distress and becomes tachypneic with a RR of 34/min. On auscultation of her chest there are crackles heard in all lung fields. Other vitals sign are T 36.8 C, P 100 bpm, and BP 90/60 mm Hg. Her O_2 saturation is 60% and she is cyanotic.

Laboratory Data: Blood draws show a hematocrit of 26%, platelet count of 135,000/mL and WBC count of 8000/mL.

Portable AP Chest X-ray reveals substantial pulmonary edema with bilateral infiltrates. An assessment is made and swift interventions are enacted in order to prevent further progression of the disease.

Case 2 Questions:

Q2.1 What is the assessment for D.L.?

Answer: Transfusion Related Acute Lung Injury (TRALI)

Q2.2 Describe the pathophysiology of the disease.

Answer: TRALI is now the leading cause for transfusion-related mortality. It is caused most often when donor plasma or PRBCs contains HLA or leukocyte (usually granulocyte) specific antibodies. Recipient leukocytes may be 'primed' by underlying illness to become more adherent to pulmonary alveolar epithelium. Introduction of the donor antibodies into the recipient causes granulocyte enzymes to be released, increasing capillary permeability and resulting in sudden respiratory distress from pulmonary edema, typically within 6 hours of transfusion. Leukopenia may transiently occur. Most cases improve within 2 days.

Q2.3 How could this have been prevented?

Answer: Use of plasma from men reduces the incidence of TRALI, since women who have been pregnant are more likely to have higher titer HLA antibodies. Using washed RBCs will remove nearly all of the plasma.

Q2.4 What type of transfusion reaction might have occurred if her temperature incrementally increased s/p transfusion?

Answer: Febrile reaction. White blood cell reactions (febrile reactions) are caused by patient antibodies directed against antigens present on transfused lymphocytes or granulocytes. Symptoms usually consist of chills and a temperature rise > 1 degree C. Risk for febrile transfusion reactions may be reduced by the usage of leukocyte reduced PRBCs.

Q2.5 What type of transfusion reaction might have occurred if she experienced pruritus and hives?

Answer: Allergic reaction. Allergic reactions to plasma proteins can range from complaints of hives and itching to anaphylaxis.

Q2.6 What type of transfusion reaction might have occurred if her urine and serum were pink?

Answer: Hemolytic reaction. Hemolytic reactions occur when the recipient's serum contains antibodies directed against the corresponding antigen found on donor red blood cells. This is most likely to be an ABO incompatibility or much less commonly an incompatibility related to a different blood group antigen. The most common cause for a major hemolytic transfusion reaction, however, is a clerical error, such as a mislabeled specimen sent to the blood bank, or not properly identifying the patient to whom you are giving the blood. A major hemolytic transfusion reaction is intravascular, depleting haptoglobin and allowing free hemoglobin to be filtered through the kidneys, producing acute tubular necrosis.

Case 2 Discussion:

Learning Objectives

1. TRALI
2. Other Transfusion Reactions

D2.1 Transfusion related acute lung injury (TRALI)

TRALI is now the leading cause for transfusion-related mortality. It is caused most often when donor plasma or PRBCs contains HLA or leukocyte (usually granulocyte) specific antibodies. Recipient leukocytes may be 'primed' by underlying illness to become more

adherent to pulmonary alveolar epithelium. Introduction of donor antibodies into the recipient causes granulocyte enzymes to be released, increasing capillary permeability and resulting in sudden respiratory distress from pulmonary edema, typically within 6 hours of transfusion. Leukopenia may transiently occur. Most cases improve within 2 days. TRALI most often occurs with administration of blood products with plasma, such as FFP. Use of plasma from men reduces the incidence of TRALI, since women who have been pregnant are more likely to have higher titer HLA antibodies.

D2.2 Other Transfusion Reactions

Hemolytic Reactions:

Hemolytic reactions occur when the recipient's serum contains antibodies directed against the corresponding antigen found on donor red blood cells. This can be an ABO incompatibility or an incompatibility related to a different blood group antigen. Disseminated intravascular coagulation (DIC), renal failure, and death are not uncommon following this type of reaction.

The most common cause for a major hemolytic transfusion reaction is a clerical error, such as a mislabeled specimen sent to the blood bank, or not properly identifying the patient to whom you are giving the blood. **DO NOT ASSUME IT IS SOMEONE ELSE'S RESPONSIBILITY TO CHECK!**

Allergic Reactions:

Allergic reactions to plasma proteins can range from complaints of hives and itching to anaphylaxis. Such reactions may occur in up to 1 in 200 transfusions of RBCs and 1 in 30 transfusions of platelets.

Febrile Reactions:

White blood cell reactions (febrile reactions) are caused by patient antibodies directed against antigens present on transfused lymphocytes or granulocytes. The risk for febrile reaction is 1 in 1,000 to 10,000.
Symptoms usually consist of chills and a temperature rise > 1 degree C.

Transfusion Associated Circulatory Overload (TACO):

Circulatory overload can occur with administration of blood or any intravenous fluid, particularly in patients with diminished cardiac function.

Case 2 References:

Hirayama F. Current understanding of allergic transfusion reactions: incidence, pathogenesis, laboratory tests, prevention and treatment. Br J Haematol. 2013;160(4):434-44.

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Case 3: Risks for infections

History: T.H. is a 30-year-old Caucasian female who is currently undergoing chemotherapy for Hodgkin Lymphoma, nodular sclerosis type, stage 2, involving her chest.

Laboratory studies last month showed her hemoglobin 8.5 g/dL with a hematocrit of 26%, platelet count 130,000/mL, and WBC count 2700/mL.

She is now getting another round of chemotherapy. While at the infusion center, she suddenly feels faint and collapses. Upon arrival in the Emergency Department, vital signs show temperature 37 C, pulse 100/min, respiratory rate 30/min, and blood pressure 100/60 lying and 80/50 mm Hg sitting.

Laboratory Data:	Patient	Normal Ranges
Hemoglobin	7 g/dL	(12.1-15.9 g/dL)
Hematocrit	21%	(34.3-46.6%)
Platelet count	10,000/mL	(177 – 408 K/mL)
WBC	1000/mL	(3.2-10.6 K/mL)
PT	14 seconds	12-15.5 seconds
INR	1.1	
PTT	25 seconds	24-35 seconds

She is admitted to the oncology ward. A cross match is ordered, and she is A positive. Two units of PRBCs are given, and she receives 6 single donor platelet units. These are transfused over the course of an hour without complication. Her post-transfusion hematocrit is 27% and platelet count 45,000/mL. Later that evening while resting, she experiences a temperature spike to 38 C, with a pulse of 122 bpm and a BP of 97/60 mm Hg. There are no signs of hemorrhage. Blood cultures are drawn, which ultimately come back positive, and a regimen of broad-spectrum antibiotics are begun.

Case 3 Questions:

Q3.1 What are the differential diagnoses?

Answer: Given her history, physical and laboratory findings, it is readily apparent that she is septic with a bacterial infection. How she got there, however, is open to debate. Although she had increased susceptibility to infection due to her immunosuppressed state from her chemotherapy treatments, given the course of disease, it is more likely that she contracted the infection directly from the transfer of blood products, with platelets being the most likely culprit.

Q3.2 Is there an increased risk for infection and/or sepsis based upon the treatments she received?

Answer: The chemotherapy treatments she had been regularly receiving have resulted in myelosuppression, with decreased formation of the normal blood cells. As a result of the decreased number of white blood cells in her serum, she is at increased risk for infection.

Conversely, the transfusion of blood products carries a risk of contamination and infection.

Q3.3 What are the risks for the blood products she received?

Answer: Bacterial contamination of blood can occur during collection. Bacteria can grow during storage at room temperature and during refrigeration (psychrophilic organisms). Platelet products carry the greatest risk, because they are stored at room temperature. Transfusing a contaminated unit can result in septic shock and death.

Q3.4 What are the risks for other infectious agents?

Answer: Some of the most common transfusion transmitted diseases are Hepatitis B virus (HBV, risk of transmission: 1 in 200,000-500,000), Hepatitis C virus (1 in 1,000,000-2,000,000), Human Immunodeficiency Virus (HIV, 1 in 1,000,000-2,000,000), Human T-lymphocytotropic virus (HTLV, 1 in 2,000,000-3,000,000), Cytomegalovirus, and Malaria.

Q3.5 What is routinely done to minimize these risks?

Answer: The risk of transmission is significantly reduced by blood screening for infectious agents and extensive questionnaires regarding travel to endemic areas or contact with persons at risk.

Q3.6 What are some emerging infections that must be considered?

Answer: Emerging diseases include Lyme disease (*Borrelia sp.)*, Babesiosis (*Babesia sp.)*, Chagas disease (*Trypanosoma* sp.) and Creutzfeldt-Jakob disease.

Case 3 Discussion:

Learning Objectives:

1. Bacterial infection with contaminated blood products
2. Transfusion transmitted diseases
3. Blood testing for infectious diseases
4. Screening for potential donors

D3.1 Bacterial infection with contaminated blood products

Bacterial contamination of blood can occur during collection. Bacteria can grow during storage at room temperature and during refrigeration (psychrophilic organisms). **Platelet products carry the greatest risk, because they are stored at room temperature**. Transfusing a contaminated unit can result in septic shock and death.

D3.2 Transfusion transmitted diseases

The following are some of the most common diseases transmitted via transfusions.

Hepatitis B

Hepatitis B virus (HBV) is transmitted through parenteral and sexual exposure. The incubation time is a mean of 90 days with a range of 30 to 180 days. Donor blood is routinely tested for HBsAg and HBcAb. **Risk of transmission (RT) = 1 in 200,000 to 500,000**

Persons who have received a hepatitis B vaccination (recommended for all health care workers with patient contact) will have hepatitis B surface antibody present, but not HBsAg or HBcAb.

There is no routine testing for hepatitis A, because it is rarely transmitted by blood products. Recipients of blood products can also be infected with hepatitis delta, which is a defective RNA virus that needs a HBV superinfection to replicate.

Hepatitis C

The route of transmission is parenteral, with sexual transmission lower than previously thought. The mean incubation time is 6 to 8 weeks. At present, only testing for hepatitis C antibody is available. **Risk of transmission (RT) = 1 in 1,000,000 to 2,000,000**

Human Immunodeficiency Virus (HIV)

The first testing of blood products for HIV started in 1985 and is a test to detect the presence of antibody directed against HIV glycoproteins and surface antigens. Testing for HIV p24 antigen was mandated in 1996. **Risk of transmission = 1 in 1,000,000 to 2,000,000**

Human T-lymphocytotropic Virus (HTLV-I/II)

HTLV-1 is a retrovirus that is endemic in Japan and the Caribbean. Implicated as causing adult T-cell leukemia/lymphoma and a neurological disorder similar to multiple sclerosis. Blood is routinely screened for antibodies to HTLV-I. **Risk of transmission = 1 in 2,000,000 t0 3,000,000** (but only 1-3% of seropositive individuals will develop disease).

Cytomegalovirus (CMV)

The prevalence of CMV antibody ranges from 50 to 80% of the population. Blood contaminated with CMV can cause problems in neonates or immunocompromised patients. Potential problems in selected patient populations can be prevented by transfusing CMV negative blood or frozen, deglycerolized RBC's. **Donor blood is not routinely tested for CMV.**

Malaria

Malaria is rarely transmitted by RBC products, although the number of transfusion associated cases of malaria is at an all-time high. **Donors traveling to high risk malaria areas are excluded from donating blood for six months.** In areas of high prevalence, an antibody test to detect *Plasmodium falciparum* and *Plasmodium vivax* can be employed.

Additional diseases which are rarely transmitted by blood products include:

- Lyme disease (*Borrelia sp.*)
- Dengue fever
- Babesiosis (*Babesia sp.)*
- Chagas disease (*Trypanosoma cruzi*)
- Creutzfeldt-Jakob disease

Potential donors may be screened by questionnaire regarding travel to endemic areas or contact with persons at risk. Antibody tests available for all but babesiosis and CJD are available, preferentially applied in regions of high prevalence.

D3.3 Blood testing for infectious diseases

A number of laboratory tests must be completed before blood or blood products can be transfused:

- Determination of the blood type with a crossmatch.
- Screening for antibodies that may produce adverse effects if transfused.
- Screening for possible infectious agents that could be transmitted with transfusion.

The following tests are mandatory on all units of blood collected for transfusion:

- **ABO group and Rh type**
- **Screening for blood-group antibodies**

Serologic tests for human retroviruses including:

- HIV-1
- HIV-2
- HTLV I
- HTLV II

Serologic tests for viral hepatitis including:

- Hepatitis B
- Hepatitis C

Serologic tests for additional infectious agents including:

- Syphilis (Treponema pallidum)
- West Nile virus
- Chagas disease (Trypanosoma cruzi)

If, and only if, all of these markers are negative can blood be conveyed to the Blood Bank for storage until usage. A positive results for some of these tests may prevent further donation by that person. A person with such a test result will be notified by the donor center. Persons with a potential medical condition should see a physician and should not, under any circumstance, donate only to have blood tested. These measures are done to make the blood supply as safe as possible.

D3.4 Screening for potential donors

In order to insure patient safety, potential donors undergo thorough screening in order to eliminate unsuitable candidates. Criteria that must be satisfied before donation

include:

- Medical history, with an acceptable hemoglobin level and no current prescriptions that may cause problems when donating
- Good physical health and feeling well on the day of donation
- Possible contact with transfusion-transmissible infectious diseases through sexual history, drug use and travel
- Photo identification
- At least 56 days have passed since prior donation.

These criteria are covered in a complete health questionnaire and confidential interview that must be completed during each donation. Failure to follow strict adherence to the established protocol increases the risk for injury to potential recipients.

Case 3 References:

Dodd RY. Emerging pathogens and their implications for the blood supply and transfusion transmitted infections. Br J Haematol. 2012;159(2):135-42.

Lindholm PF, Annen K, Ramsey G. Approaches to minimize infection risk in blood banking and transfusion practice. Infect Disord Drug Targets. 2011;11(1):45-56.

Schmidt M, Geilenkeuser WJ, Sireis W, Seifried E, Hourfar K. Emerging Pathogens - How Safe is Blood? Transfus Med Hemother. 2014;41(1):10-17.

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Case 4: Hemolytic Disease of the Newborn (erythroblastosis fetalis)

History: E.P. is a 27 year-old Asian G3, P2 who is currently 36 weeks pregnant. Her first pregnancy was uneventful and ended with the birth of a healthy male at term. Her second pregnancy, however, ended 3 weeks prematurely with the birth of female infant with mild neonatal jaundice that responded to phototherapy. Blood typing of the mother at that time revealed she was blood type A Rh (+). However, her spouse was blood type O Rh (-).

Now in her third pregnancy, E.P. has an uneventful prenatal course. A Coombs test is negative. She gives birth at 38 weeks to a neonate that is not jaundiced. However, the delivery is not without complications. The placenta cannot be delivered. She experiences massive hemorrhaging due to placenta accreta, and her hematocrit falls to 20%.

Other Laboratory Data:	Patient	Normal Ranges
Hemoglobin	6.4 g/dL	(12.1-15.9 g/dL)
Platelet count	200 K/mL	(177-408 K/mL)
WBC	8 K/mL	(3.2-10.6 K/mL)
PT	12 seconds	12-15.5 seconds
INR	1.0	
PTT	24 seconds	24-35 seconds

While being crossmatched for PRBCs, 6 of 10 units are found to incompatible. A comprehensive workup is done for irregular antibodies.

Case 4 Questions:

Q4.1 What is the assessment?

Answer: Maternal serum with irregular antibodies due to alloimmunization from previous pregnancies. The most recent pregnancy was not complicated by erythroblastosis fetalis, but the second pregnancy was.

Q4.2 What was the role of the prior pregnancies in contributing to the formation of the irregular antibodies?

Answer: Previous pregnancies exposed the mother to novel (paternally derived) antigens, which resulted in the formation of irregular antibodies by the mother that can cross the placenta and attack fetal red blood cells that have these surface antigens.

Q4.3 What is the most common alloimmunization associated with pregnancy? How can it be prevented?

Answer: The most common alloimmunization associated with pregnancy is the exposure of maternal Rh D (-) blood to fetal Rh D (+) blood. This results in the production of maternal IgG against the "D" antigen that can cross the placenta and attack fetal red blood cells, resulting in hemolytic disease of the newborn. This can be prevented by the use of Rho(D) immune globulin, commonly known as RhoGAM. RhoGAM consists of IgG anti-D antibodies that will help neutralize the antigen and prevent the mother's immune system from sensitization to the antigen, and preventing the immune response that generates the alloantibodies.

The use of RhoGAM and greatly reduced the incidence of Rh anti-D erythroblastosis fetalis, and so other blood group antigens, such as Kell, may be implicated, as in this case.

Q4.4 Describe the process of obtaining compatible blood. How is blood obtained for persons with rare blood types?

Answer: If an alloantibody is detected, then RBC units may be crossmatched randomly, assuming that the alloantibody is against a "low incidence" antigen which most units will lack. Chances are, enough compatible units will be identified.

If an alloantibody is directed at a "high incidence" antigen, then there will be few, if any, units available that match. In that case, "rare" blood units lacking the antigen may be requested from a facility that stores such blood. Cryopreservation of RBCs is done to store special, rare RBCs for up to 10 years in a glycerol solution. The thawed units are washed of the glycerol, and by doing so are also depleted of plasma and leukocytes.

However, the process of identifying alloantibodies and finding compatible blood is time consuming.

Case 4 Discussion:

Learning Objectives

1. Alloimmunization
2. Hemolytic Disease of the Newborn (erythroblastosis fetalis)
3. Graft Versus Host Disease (GVHD)
4. Blood Compatibility Testing

D4.1 Alloimmunization

Alloimmunization, which is an immune response to foreign antigens from the same

species, can occur with the transfusion of PRBCs and platelets.

PRBCs
RBC transfusions can expose the patient to RBC antigens not recognized as self. If an antibody is produced, future transfusions can be delayed because extended donor blood typing will be required to identify compatible units.
O negative blood released uncrossmatched in emergencies could result in a hemolytic transfusion reaction if the patient has an alloantibody produced after a previous transfusion.
Alloantibody production in a female can result in hemolytic disease of the newborn.

Platelets
Platelets contain HLA and A & B antigens. Prior exposure to non-self HLA antigens (from WBC contamination of red cell products) can result in antibodies that will render future platelet transfusions useless.

D4.2 Hemolytic Disease of the Newborn

Maternal IgG antibodies can cross the placenta and provide the fetus with passive immunity following birth. However, these antibodies could be directed at antigens on fetal cells. When directed at red blood cell antigens, then hemolysis can occur, with fetal hydrops and/or neonatal jaundice.

Both major (A and B) and minor (Rh and others) antigens may be targeted. There is usually little IgG directed at major A and B antigens, so maternal-fetal ABO incompatibility is usually nonexistent or mild. However, maternal exposure to Rh antigens, typically with prior pregnancy, or prior transfusion, can induce higher IgG titers that can lead to significant hemolysis pre and postnatally in subsequent pregnancies. Most cases are due to antibodies to the "D" antigen, termed "Rh Positive." The Rh negative mother forms antibodies on exposure to Rh positive RBCs. However, antibodies may also be directed at other Rh antigens and other minor blood group antigens such as Kell.

Screening for these alloantibodies can be done with a Coombs test. To prevent alloimmunization at the time of birth, when fetal-maternal hemorrhage may occur, exposing the mother to fetal RBC antigens, the product RhoGAM (Rh(D) immune globulin) can be given.

D4.3 Graft Versus Host Disease (GVHD)

GVHD is a situation where transfused lymphocytes engraft and multiply in immunocompromised patients (e.g., bone marrow transplant patients). The newly engrafted lymphocytes attack the host. This is the opposite of a host rejecting a transplanted organ (e.g., a heart).

Transfusion-associated graft versus host disease (TAGVHD) is a different disease from GVHD in allogeneic bone marrow transplant recipients. TAGVHD is uniformly fatal and

untreatable. It occurs in immunocompromised patients when the blood products contain T-lymphocytes and attack many host tissues.

TAGHVD is prevented by gamma-irradiating the blood products to be transfused.

D4.4 Blood Compatibility Testing

Blood Type

A "type" includes a "front type" and a "back type". The "front type" determines which antigens ("flags") in the ABO blood group system are on the patient's red blood cells as follows:

Antigen	Blood Type
A antigen only	Type A
B antigen only	Type B
A and B antigens	Type AB
Neither A or B	Type O

The "back type" identifies the isohemagglutinin (naturally occurring antibody) in the patient's serum and should correspond to the antigens found on the red blood cells as follows:

Antibody	Blood Type
anti-B	Type A
anti-A	Type B
anti-A and anti-B	Type O
Neither anti-A or anti-B	Type AB

Blood Type O is considered to be a "Universal Donor" in that it lacks both major ABO antigens, while AB is the "Universal Recipient" in that it has both major antigens but lacks antibodies to A and B.
In addition, RBC's are Rh typed and identified as "D" positive or negative.

Crossmatching

The patient's blood is typed for the blood type and then a "screen" looks for unexpected red cell alloantibodies which may form following pregnancy or prior transfusions. If the screen is positive, the antibody needs to be identified. The physician is also notified. **Antibody identification can be complicated and take more than a day to complete.**

"Type and Screen"

This procedure is ordered when it is unlikely that blood will be needed emergently. There are no donor units specifically matched for the patient and reserved for the patient. However, the patient's blood type is identified, and a screen will have identified

any potential antibodies that could complicated obtaining blood. A crossmatch to find compatible units can be done more easily following a "type and screen."

"Type and Cross"

A "type and cross" is ordered when it is likely that blood will be needed. Compatibility testing between patient and donor units is performed and at least 2 units are crossmatched for the patient and reserved specifically for that patient. These units cannot be used for anyone else. If they are not used, then they can go back into the inventory for use by others.

- **A full crossmatch procedure takes about 45 minutes to complete and cannot be shortened.**

- Units are refrigerated until used.

- A unit of blood must be properly labeled and the label MUST be checked before use. Every unit crossmatched to a patient is removed from the general inventory and reserved for the patient for 72 hours. **Units which are crossmatched unnecessarily will deplete Blood Bank inventories and can result in blood shortages.** Blood shortages can result in cancellation of elective surgical procedures.
Blood will ordinarily not be released for transfusion until compatibility testing is completed. However, under emergency conditions, blood products may be released without a crossmatch if the patient is in danger of dying if transfusion is delayed. In such cases, if the patient's blood type is not known, then group O Rh negative (O neg) blood can be released without compatibility testing. In cases in which the patient's blood type is reliably known, then type-specific blood of the same ABO and Rh group may be released.

Case 4 References:

Fast LD. Developments in the prevention of transfusion-associated graft-versus-host disease. Br J Haematol. 2012;158(5):563-8.

Moise KJ Jr, Argoti PS. Management and prevention of red cell alloimmunization in pregnancy: a systematic review. Obstet Gynecol. 2012;120(5):1132-9.

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Case 5: Therapeutic Apheresis

History: A 57-year-old African-American previously healthy male has been experiencing malaise and increasing weakness upon exertion for the last 3 months. He has difficulty keeping his eyes open, along with diplopia, by the end of the day. He feels better, with more strength, following a night's sleep. He has no other major medical problems.

He suddenly experiences difficulty breathing and is brought into the Emergency Department by EMS. Vital signs are T 36 C, P 90 bpm, BP 130/95 mm Hg, and RR 32/min. Oxygen saturation is decreased and a workup is begun for COPD.

Imaging Studies: A portable AP chest X-ray is normal with sparse infiltrates, but the lateral view has a suspicious shadowing in the anterior mediastinum. A subsequent CT is done, and a large, anterior mediastinal mass is visualized.

Laboratory Data: A CBC reveals a WBC WNL, but the automated differential shows an increasingly large percentage of lymphocytes. Further testing finds a high titer of anti-AchR IgG.

His respiratory status worsens, and he is placed on a ventilator.

Case 5 Questions:

Q5.1 What is the assessment?

Answer: Myasthenia gravis crisis

Q5.2 What is the mass?

Answer: It is most likely a thymoma. These neoplasms may be benign or malignant, with benign being most likely of the two.

Q5.3 What emergent blood treatment is most indicated?

Answer: Apheresis is done to remove a component of the blood which contributes to a disease state. In this case, plasmapheresis was indicated to remove the patient's plasma (and replacement with saline solution) to reduce circulating antibodies against nicotinic Acetylcholine (Ach) receptors at the neuromuscular junction, which accounted for the symptomatic manifestation of myasthenia gravis as muscular weakness.

Q5.4 For what are other conditions could this therapy be used?

Answer: Apheresis and, more specifically, plasmapheresis can also be used therapeutically for the treatment of Waldenstrom's macroglobulinemia, Guillain-Barré syndrome, Hyperviscosity Syndromes, Paraproteinemia, Cryoglobulinemia and Goodpasture's syndrome.

Q5.5 What blood product is often obtained using the method for this therapy?

Answer: Platelets are often collected via plateletpheresis. Enough platelets can be collected at one time to equal roughly 6 single donor unit collections. This "platelet pack" can be MHC (HLA) typed and used for persons who have a platelet alloantibody, or who are likely to require multiple platelet transfusions and are at increased risk for alloimmunization if many single donor units were transfused.

Case 5 Discussion:

Learning Objectives

1. Apheresis
2. Therapeutic Apheresis

D5.1 Apheresis

The process of apheresis involves removal of whole blood from a patient or donor. Within an instrument that is essentially designed as a centrifuge, the components of whole blood are separated. One of the separated portions is then withdrawn and the remaining components are retransfused into the patient or donor.

The components which are separated and withdrawn include:

- Plasma (plasmapheresis)
- Platelets (plateletpheresis)
- Leukocytes (leukapheresis)

D5.2 Therapeutic Apheresis

The purpose of therapeutic apheresis is to remove a component of the blood which contributes to a disease state. Examples include:

Plasmapheresis

Within the plasma are contained antibodies and antigen-antibody complexes that may contribute to the deleterious effects of autoimmune diseases. Removal of the plasma (and replacement with saline solution) will help to reduce circulating antibodies and immune complexes. In rare circumstances, excess blood proteins are present that may cause circulatory problems. Examples of these diseases include:

- Waldenstrom's macroglobulinemia
- Myasthenia gravis
- Guillain-Barré syndrome
- Hyperviscosity Syndromes
- Paraproteinemia
- Cryoglobulinemia
- Goodpasture's syndrome

Plateletpheresis

Rarely, in myeloproliferative disorders, the platelet count can be very high (thrombocytosis). Removal of platelets can help to avoid complications of thrombosis and bleeding.

Leukapheresis

In some cases of leukemia with very high white blood cell counts, removal of the excess leukocytes may help to prevent complications of thrombosis.

Stem Cell Harvesting

The small number of circulating bone marrow stem cells can be harvested to use in hematopoietic stem cell transplantation procedures.

Case 5 <u>References:</u>

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