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Blood Transfusions: Friend or Foe?
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Disclosures
• none

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Objectives
• Describe the pathophysiology required for safe administration of blood products.
• Review the implications and complications of blood product administration.
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Introduction

• Transfusions have been used for over 50 years.
• Approximate 30 million blood components are transfused yearly in the US.*
• Transfusion has come under increased scrutiny over last 20 years.


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Reasons for ICU Anemia

Phlebotomy
– 20% total blood loss
– Avg discard 10cc
– CT ICU - 377cc
– A-Lines >

GI Losses
Surgical Procedures


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Prevalence of Anemia

• 95% of ICU patients below normal by ICU day 3
• 50% of ICU patients received at least 1 unit pRBCs
• 85% of ICU patients who remained in the ICU more than one week received at least 1 pRBC

Vincent JL et al. JAMA 2002;228:1499-507
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**Banked Whole Blood**

- No components have been removed.
- Consists of RBCs, WBCs, and platelets (plts) in plasma.
- Can be stored for 5 weeks.
- Transfusions of whole blood are rarely required (only in massive blood transfusion).
- Stored in the refrigerator, the platelets are useless and factors V and VIII are greatly reduced.

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**Banked Whole Blood**

- Transfusion of whole blood might be necessary...
  - in certain types of major surgery
  - major trauma requiring emergency surgery
- Acute blood loss > 15%

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**Fresh Whole Blood**

- Blood that is administered within 24 hours of its donation.
- Rarely indicated.
- Poor source of platelets and Factor VIII.
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Blood Component Therapy

- The process of transfusing only that portion of the blood needed by the patient.
- It allows a single unit (one pint) of donated blood to benefit more than one patient.
- RBCs and plts are the most frequently transfused blood components.

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pRBCs

- The red cells from a donor unit, diluted with plasma to a hematocrit of about 75%.
- Each unit of pRBCs has a total volume of 300 ml, of which ~200 ml are RBCs.
- Storing red cells (just above freezing) allows survival for about 42 days – but unfortunately decreased 2,3-DPG – ruins the platelets and neutrophils

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pRBCs

- Product of choice for most clinical situations.
- Fastest way to increase the oxygen-delivering capacity of the blood.
- A unit of whole blood or packed RBCs will raise the hematocrit by 3% and the hemoglobin by 1-1.5 gm/dL.
Leukoreduction

- Removal of leukocytes
- Costly
- Preferred for the following patients:
  - chronically transfused patients
  - potential transplant recipients
  - patients with previous transfusion reactions
  - Patients undergoing cardiopulmonary bypass
  - CMV seronegative patients who are at risk for CMV infection

Autotransfusion

- Collection of a patient’s blood during acute blood loss, followed by transfusion of the blood back to the patient.
- Acceptable to some Jehovah’s Witnesses.*
- Usually limited to less than 10-15 L if possible.
- Blood generally collected from chest tubes or aspirated from pleural and peritoneal cavities.

Frozen RBCs

- Reduces the risk of infusing antigens or foreign bodies, that the body might regard as potentially dangerous.
- Not available for use in emergency situations.
- RBC viability is improved.
- ADP and 2,3 DPG maintained.

Plasma Products

- Plasma is the portion of whole blood that remains after RBCs, WBCs, and platelets have been removed by centrifugation.
- Preparations include:
  - FFP
  - Cryo
  - Factor concentrates
  - IVIG

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FFP

- From freshly donated blood.
- Source of vitamin K-dependent clotting factors.
- Only source of Factor V.
- Indications:
  - For coagulopathy and deficient clotting factors:
    - 1 unit FFP = 3% increase in CF levels
    - At least 30% to ensure adequate coagulation

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Cryoprecipitate

- Prepared from plasma
- Rich in clotting factors
- Indications:
  - Hemophilia
  - Von Willebrand's disease
  - Other major coagulation abnormalities
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**Factor Concentrates**

- Produced with recombinant technology OR collected from thousands of donors and pooled into a highly concentrated product.
- Some coagulation factor concentrates have been available for years.
  - Factor VIII for hemophilia A
  - Factor IX for hemophilia B

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**Factor Concentrates**

- **PCC** (prothrombin complex concentrates)
  - Overall clotting factor concentration is approximately 25 times higher than in normal plasma.
  - Includes Factors II, VII, IX, X, Proteins C and S, Antithrombin II and human albumin

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**IVIG**

- The purified immunoglobulin fraction of plasma pooled from several thousand donors
- Useful in the treatment of some autoimmune and immunodeficiency states.
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**Platelet Concentrates**

- **Components:** platelets, 50 ml plasma
- Cellular components that help in the clotting process.
- Platelets must be stored at room temperature (so are only good for up to 5 days).
- One unit will usually raise the platelet count 5-10k/microliter.
- Check one hour after transfusion.
  - If the platelet count does not increase as expected, suspect DIC or immune platelet destruction (anti-HLA)
- **Indications:**
  - Used if there is a platelet disorder
  - When massive blood loss has occurred

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**Serologic compatibility**

- Type and cross VS type and screen:
  - “Type and cross” is usually requested when the potential for blood use is high (e.g., trauma, open heart surgery, etc). The physician will request a crossmatch along with an ABO/Rh blood type and antibody screen. In the crossmatch, the patient’s blood and donor blood are tested for compatibility.
  - “Type and screen” may be requested in circumstances not likely to require transfusion, such as elective surgery. The patient’s ABO/Rh blood type is determined, and an antibody screen is done. No blood is crossmatched.

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**Crossmatching blood**

- **Type and cross VS type and screen:**
  - “Type and cross” is usually requested when the potential for blood use is high (e.g., trauma, open heart surgery, etc). The physician will request a crossmatch along with an ABO/Rh blood type and antibody screen. In the crossmatch, the patient’s blood and donor blood are tested for compatibility.
  - “Type and screen” may be requested in circumstances not likely to require transfusion, such as elective surgery. The patient’s ABO/Rh blood type is determined, and an antibody screen is done. No blood is crossmatched.
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O negative blood

• Universality and timely availability from hospital blood banks
• When used during massive exsanguination is potential problems with crossmatching and incompatibility later in the patient’s hospital stay
  – More than 4 units

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O positive blood

• Has been shown to be generally safe and can help prevent blood shortages
• Administer to men and postmenopausal women
• To women of childbearing age, can result in sensitization

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Rh groups

• Rh negative recipients should be transfused with Rh negative blood.
• Rh negative group
  – 15% of the population
  – Limited supply
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Risks and Complications

- Immunologic reactions
- Volume overload
- Hypothermia
- Coagulopathy
- Citrate toxicity
- Acute lung injury
- Posttransfusion purpura

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Risks and Complications

- Infection
  - Viruses, bacteria, and parasites can be transmitted.
  - Transfusion-mediated immunosuppression may lead to increased risk of postoperative bacterial infection

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Transfusion-related mortality

- FDA reported 59 transfusion-related or potentially transfusion-related deaths in 2014.
- Transfusion-related deaths from 2009-2013:
  - TRALI 38%
  - TACO 24%
  - Hemolytic reactions 22%
  - Microbial infections 19%
  - Anaphylactic reactions 5%

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Transfusion Reactions:
• Hemolytic reactions (acute or delayed)
• Allergic reactions
• Febrile reactions
• Immunomodulation

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Hemolytic Reactions
• Transfusion of an incompatible blood component
• Most are due to naturally occurring antibodies in the ABO antigen system and Rh groups
• May cause hemoglobin induced renal failure and a consumptive coagulopathy (DIC).

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Hemolytic Reactions

Acute
• Occur in about 0.016% of RBC transfusions
  - Pain at infusion site
  - Fever
  - Chills
  - Back and substernal pain
  - Renal failure changes
  - Dysepsa
  - Hypotension
  - Elevated JVP
  - Cyanosis
  - Coagulopathy due to DIC

Delayed
• Occur in about 0.025% of RBC transfusions
• Often mild and may be undetected
• Pregnant women and previously transfused pts at highest risk
  • S/S:
    - Jaundice
    - Hemoglobinuria
    - Falling hemoglobin concentration
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**Hemolytic/Transfusion Reaction**

*Most dangerous!*

Develops within first 15 minutes of transfusion: free hemoglobin in blood and urine specimens provide evidence of acute hemolytic reaction; delayed at 2-14 days

Occurs after 100-200 ml blood infused!

**Blood incompatibility**

- RBC's clump (lysis of RBC's), block capillaries, decrease blood flow to organs.
- Hgb released (myogloburia), blocks renal tubules > acute renal failure=ATN (acute tubular necrosis)
- Fever/chills
- SOB/dyspnea/wheezing
- Apprehension
- Headache/low back pain
- Chest pain/chest tightness
- Urticaria/tachycardia
- *Hematuria

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**Hemolytic/Transfusion Reaction**

If hemolytic reaction occurs:

- Stop transfusion, keep IV line open with new tubing, saline, colloid solution to maintain BP; monitor
- Notify MD of patient signs and symptoms
- Treat shock (anaphylactic) if present (epinephrine, oxygen, antihistamines, vasopressors, fluids, corticosteroids)
- Draw blood samples for serologic testing; send urine to lab and return blood tubing to blood bank for testing
- Prevent acute renal failure: give diuretic, fluid challenge

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**Allergic/urticarial transfusion reactions**

- Most common usually due to allergies to specific proteins in the donor’s plasma
- Can be avoided with future transfusions by pretreatment with antihistamines or steroids
- Some pts get “hay fever/hives/wheezing” from transfusions (pre-treat with antihistamine)
Allergic/urticarial transfusion reactions

- For severe (anaphylaxis), RBCs and platelets are washed to remove all plasma
  - Very fast onset after transfusion of only a few mls
  - IgA deficiency should be considered in the case of anaphylactic reactions.

Delayed hemolytic transfusion reactions

- 1 in ~6000; fatality rate 0.1%
- Previously sensitized to an antigen through transfusion or pregnancy
- Can result in symptomatic or asymptomatic hemolysis several days (2-10 days) after a subsequent transfusion.
- Not preventable.
- A new antibody or anamnestic response has probably developed.

Delayed hemolytic transfusion reactions

- Most frequent: Transfusion of Rh positive RBCs to an Rh negative woman of childbearing age can result in sensitization and hemolytic disease of the newborn in future pregnancies.
Transfusion Related Acute Lung Injury (TRALI)

- "noncardiogenic pulmonary edema"
- Defined to be ARDS within 6 hours of a transfusion with no other clear cause.
- Occurs when donor plasma contains an antibody, usually against the patient’s HLA or leukocyte specific antigens.

- 1 in 1000; fatality rate <1% with estimates varying widely.
- The cause is apparently antibodies in the donor plasma against the patient’s neutrophils (which, in the sick, are marginated in the lung vessels).
- The donor antibodies cause these neutrophils to release toxic products and thus produce ARDS.

Clinical presentation
- Dyspnea, hypotension, fever typically begin 30 minutes to 5 hours after transfusion.
- Chest x-ray shows diffuse non-specific infiltrates, “white out”
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**Transfusion Related Acute Lung Injury (TRALI) Treatment**

- Therapy is primarily supportive
- Ventilatory support may be required for several days before resolution.

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**TACO**

- Volume overload (transfusion-associated circulatory overload—TACO)
  - Pulmonary edema secondary to congestive failure
  - Risk factors include older age, cardiac and renal dysfunction, chronic anemia, increased rate of transfusion.

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**TACO**

- In 2010, TACO was second most common cause of transfusion-related mortality
  - Occurs in 1:100 or 1:10,000.
  - More likely to occur with pRBCs or FFP d/t high volume.
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**Bacterial Contamination**

- Rare
- Acquired from contaminated collection bags d/t poor cleaning of donor’s skin
- Reactions are quite severe with high fever, rigors and/or other systemic symptoms such as hypotension, nausea, or vomiting.
- Pseudomonas most common.
- Platelets (kept at room temp during their 5-day shelf life) are a great culture medium.
- Transfusion should be stoped and the bag sent for gram stain and culture.
- The blood center/bank should be notified.
- The patient should have blood cultures obtained and, if appropriate, IV antibiotic therapy begun.

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**Transmission of disease**

- Malaria
- CMV
- Hepatitis C and HIV
  - Dramatically decrease
    - Better antibody and nucleic acid screening
    - 1 per 1,000,000 units
- Hepatitis B
  - 1 per 100,000 units
- Hepatitis A
  - Very rare, no asymptomatic carrier state

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**Pathogen Inactivation Technology**

- For platelets and plasma use the small molecule amotosalen HCl which penetrates cells and pathogens and targets DNA and RNA.
- Once docked inside DNA and RNA, amotosalen is activated by UV light to form a chemical crosslink that locks-up the strands of nucleic acid, blocking replication.
- For red cells uses a different molecule (S-303) that forms crosslinks when activated by a change in pH.
- Treated pathogens are inactivated by the process and can no longer multiply and cause disease.
Transfusion Thresholds

- No single measure can replace good clinical judgment as the basis for decision-making regarding perioperative transfusion!!
- Mild-to-moderate anemia does not contribute to perioperative morbidity.

TRICC (Transfusion Requirement in Critical Care)

- Compared liberal (target Hgb 10-12) vs restrictive (hgb 7-9) transfusion policy in 838 euvoletic pts with Hgb<9 within 72 hours of ICU admission.
- Restrictive strategy was superior for pts <55 and with lower (<20) APACHE II scores.
- Liberal transfusion was not superior.

Society of Critical Care Medicine/Eastern Association for Surgery of Trauma (2007)

- Indicated in hemorrhagic shock
- May be indicated in acute hemorrhage and hemodynamic instability or inadequate O2 delivery
- Transfusion at HGB<7 is as effective as at HGB<10 in critically ill, hemodynamically stable patients.
- May be benefical in ACS with HGB<8 on admission.
Blood loss of 1L in a healthy adult

- Venous hematocrit fall by...
  - 3% in the first hour
  - 5% at 24 hours
  - 6% at 48 hours
  - 8% at 72 hours

Massive transfusion

- Definition: Transfusion of more than total blood volume or ≥ 10 units pRBCs within a 24 hour period

Massive transfusion complications

- Coagulopathy is caused by a dilutional effect on the host’s clotting factors and platelets, as well as the lack of platelets and clotting factors in pRBCs.
- Volume overload
- Hypothermia
Massive transfusion complications

• Hyperkalemia may be caused by lysis of stored red cells
• Metabolic acidosis and hypokalemia may be caused by the transfusion of a large amount of citrated cells.
• Hypocalcemia due to citrate toxicity may occur in those with hepatic failure, CHF, or other low output states
  – Increasing uncommon with the use of component therapy

Use of blood from multiple donors increases the risk of hemolytic reactions as a consequence on incompatibility

Jehovah’s Witnesses cannot accept donor pRBCs, platelets, white cells or plasma, and cannot accept autologous or cell-cycled intraoperative transfusion.

The sect leadership used to be militantly anti-immunization, anti-germ theory, and anti-transplantation as well.