Seeing Red

Complications Associated with Blood Transfusions

Objectives
At the end of this session the participant will be able to:
1. Describe medical conditions that result in blood loss
2. Identify what patients are receiving blood products
3. Discuss the potential risks of transfusion
4. Communicate physiologic indices for transfusion and potential alternative therapy

Why Give Blood?
• Restore volume
• Improve DO2
• Improve microcirculation

Blood Transfusion
• Increasing transfusions
• Over 13 million units transfused in U.S.
• Cost of blood had doubled in past decade

Incidence
• Patients in the hospital receiving blood transfusions
  • 9% of patients in the step down unit
  • 27% of patients in the ICU
• 85% of patients with an ICU stay > 1 week will receive a blood transfusion

Blood Transfusion
• At Loyola in FY17
  • 18,201 RBC units transfused
    • (50 units per day, 7 days a week)
  • 5,550 FFP units
  • 21,838 random-donor platelets
  • 1,214 single-donor apheresis platelets
  • 3,259 cryoprecipitate

JAMA 2015
LUMC Blood Bank, Dr. DeChristopher, Medical Director
**Blood Transfusion**

- At Loyola in FY17
  - $8,415,000 direct cost for purchase of blood components
    - Not including staff, supplies, reagents, equipment
  - Lifesource direct costs
    - RBC $165
    - Leukoreduced RBC $205
    - Platelets $52 (5 are pooled for an adult dose)
    - FFP $59
    - Apheresis (single-donor) $490

**How Did This All Start?**

First scientifically recorded blood transfusion from animal to animal: 1665 – presented at a meeting of the Royal Society of London by Dr. Christopher Wren.

Paris, 1667: first ever blood transfusion from animal to human by Jean-Baptist Denis. Outcome was fatal.

1818 London- Dr. James Blundell reports on benefit of transfusion in cases of post-partum hemorrhage. He later devised Blundell’s impellor-funnel and pump for collection of donor blood for infusion into the vein of recipient indirectly.

1864- France and England- direct human-to-human transfusions performed using India rubber tubes.

1883-1884- Dr. J. Braxton-Hicks mixed sodium phosphate with blood to overcome clotting problem. All patients died.

1901 and 1902- Karl Landsteiner described 4 types of human blood.

Development of BT practices became accelerated during WWI and II. First blood bank was described in 1918.

Landsteiner is known as father of transfusion therapy.
Although cross-matching was described by Ottenburg and Kalinski in Mount Sinai Hospital in NYC in 1913 this practice was not instituted until 1950s.

By mid-60s in addition to blood grouping and AB testing microbiological testing was established, initially for syphilis only, and later for Hepatitis B, CMV and then HIV.

“Resuscitare”... Treating the Shock
- Latin – to reanimate or revive
- Refers to the diagnostic and therapeutic maneuvers used to treat trauma patients
- Defines restoration of physiologic parameters
- Reversal of shock

The Good, the Bad, and the Ugly

Where is it Lost?
- External Losses
- Impaired production
- Sequestration and increased destruction

External Losses
- Hospitalized patients are phlebotomized about 25-40mL of blood per day
- Patients with indwelling catheters can lose 900mL during their hospital stay
- Surgical/Trauma patients blood loss due to operation or injury
- GI bleeding or other bleeding sources

It Can Sneak Up On You!
- Fractures:  
  - Rib: 100-200 cc
  - Femur: 800-1200 cc
  - Pelvis: > 1500 cc
- Chest cavity: > 1500 cc
- Retroperitoneum: > 1500 cc
- Peds small margin of error: 1 year old child loses “3/4 cup” of blood is 25% blood loss class II/III shock
Impaired Production

- Hgb, MCV
- Microcytic anemias
  - Iron deficiency
  - Thalassemia
  - Chronic inflammation
  - Sideroblastic anemias
- Macrocytic anemias
  - B12, folate deficiency
  - Pernicious anemia

Impaired Production

- RBC cell production in the ill and compromised is abnormal
  - Decreased production of erythropoietin independent of acute renal failure
  - Impaired bone marrow response to erythropoietin
  - Decrease in the supply of the building blocks of blood production

Anemia of Inflammation

- Body’s response to infection
  - Down-regulate erythropoietin production and iron metabolism as a non-specific immunity
  - Starve the pathogen of iron

Sequestration and Increased Destruction

- Reduced RBC survival
- Sequestration and destruction in the spleen

Does Your Patient Need Blood?

Goal is Optimization of Tissue Perfusion

- Level of consciousness
- Skin color and temperature
- Pulse rate and character

Classes of Shock

<table>
<thead>
<tr>
<th>Blood Loss mL</th>
<th>Class I</th>
<th>Class II</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 750</td>
<td>750-1500</td>
<td>1500-2000</td>
<td></td>
</tr>
<tr>
<td>Blood Loss %</td>
<td>Up to 15%</td>
<td>15-30%</td>
<td>30-40%</td>
</tr>
<tr>
<td>Pulse rate</td>
<td>&lt;100</td>
<td>&gt;100</td>
<td>&gt;120</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>Normal</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>Pulse pressure</td>
<td>Normal</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>14-20</td>
<td>20-30</td>
<td>30-40</td>
</tr>
<tr>
<td>Urine output</td>
<td>&gt;30</td>
<td>20-30</td>
<td>5-15</td>
</tr>
<tr>
<td>Mental status</td>
<td>Slightly anxious</td>
<td>Mildly anxious</td>
<td>Anxious, confused</td>
</tr>
<tr>
<td>Fluid (3:1 rule)</td>
<td>Crystalloid</td>
<td>Crystalloid</td>
<td>Crystalloid and blood</td>
</tr>
</tbody>
</table>

Classes of Shock:

- Class I: Blood Loss < 500 mL
  - Pulse rate < 120
  - Systolic blood pressure Normal
  - Respiratory rate 14-20
  - Urine output >30
- Class II: 500 mL < Blood Loss < 1500 mL
  - Pulse rate > 120
  - Systolic blood pressure Decreased
  - Respiratory rate 20-30
  - Urine output 20-30
- Class III: Blood Loss > 1500 mL
  - Pulse rate > 120
  - Systolic blood pressure Decreased
  - Respiratory rate 30-40
  - Urine output < 20

- Slightly anxious
- Mildly anxious
- Anxious, confused
- Confused, lethargic
- Negligible
- Elevated lactate
- Decreased oxygen delivery
- Increased oxygen extraction

**Physical Symptoms**
- Tachycardia
- Tachypnea
- DOE
- Signs of hypovolemic

**Physiologic Variability**
(5/15)

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**What happens when a blood transfusion is given?**

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**What IS A Unit of Blood**

- ~300cc volume
- ~200cc RBC
- Will raise HCT 3-4%
- Will raise HBG 1 gm/l

---

**Americans donate approximately 12 million units of blood, which are processed into 20 million blood products**

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**Risks and Benefits of Blood Transfusion**

- Risk of transmission of infection
- Transfusion related immunomodulation
- Oxygen delivery and consumption?
- Transfusion errors

---

**The Beginning of the Blood Transfusion Showdown**
Reactions occur more often than recognized

- ~10%
- Types
  -- immunologic
  -- infectious
  -- chemical
  -- physiologic

The “Classic” Reaction

- Immunologic (most common)
  -- febrile non-hemolytic
  Fevers
  Chills
  Dyspnea
  -- Usually self-limiting

Risk of Transfusions

- Blood transfusions associated with
  - Infectious risk
    - Increasing safety of blood supply
      - Per unit risk for HIV is 1:1,800,000
      - Per unit risk for HCV is 1:1,600,000
      - Per unit risk for HBV is 1:220,000
    - Increasing cost of testing for infectious risk
      - Exceeds $1 million per infection prevented or QALY saved

Risk of Transfusions

Complications of Transfusions

TACO

(Transfusion Associated Circulatory Overload)

- Pulmonary edema
- Compromised patients at risk, elderly, young, cardiac history, small adults


Prevention/Treatment

- Infuse at slower rates
- Split units
- Administration of diuretics between units

TRALI

- Transfusion-related acute lung injury
  - Lung injury that occurs within 6 hours of transfusion
    - Hypoxia, dyspnea
    - Bilateral infiltrates on radiography
- Incidence
  - 0.05% per blood product transfused
  - 2% per patient transfused
- Pathophysiology
  - Donor antibodies react with recipient leukocytes
  - Recipient antibodies react with donor leukocytes


TRALI

- This reaction results in:
  - Pulmonary sequestration
  - Complement activation
  - Lung injury
- Stored blood containing cytokines IL-8 and IL-6 predispose the patient to microcirculatory capillary lung injury.

Transfusions and MOF

Hebért, et al. NEJM, 1999
Transfusion Requirements in Critical Care (TRICC)

- Prospective Randomized Trial
- Euvolemic Intensive Care Unit Patients
  - Restrictive-strategy group
    - Hbg 7-9 g/dL
    - Transfusion trigger <7.0 g/dL
  - Liberal-strategy group
    - Hbg 10-12 g/dL
    - Transfusion trigger Hbg <10.0 g/dL

TRICC Results

- 838 Canadian euvolemic intensive care unit patients enrolled
- Most common reasons for admission were respiratory and cardiac diseases
- No significant differences between the baseline characteristics of the two groups.

TRICC

- Primary outcome
  - 30-day death rates
- Secondary outcomes
  - 60-day death rates
  - ICU/Hospital mortality
  - Organ failure
  - ICU/Hospital LOS

TRICC Results

- **Restrictive Strategy** (n=418)
  - Average Hbg 8.5±0.7 g/dL
  - Red cell units given 2.6±4.1
  - 33% did not receive any blood transfusions
- **Liberal Strategy** (n=420)
  - Average Hbg 10.7±0.7 g/dL
  - Red cell units given 5.6±5.3
  - 0% did not receive any blood transfusions

*all statistically significant

**Cardiac events were more frequent in the liberal strategy group**
- Cardiac events 13.2% vs. 21.0%, p<0.01
- Pulmonary edema 5.3% vs. 10.7%, p<0.01
- No significant differences in patients 48 hours prior to death
  - Cardiac events
  - Infectious complications
  - Multiple organ failure
TRICC Conclusions

**Bottom Line - No difference in mortality and in some instances worsened morbidity**
- No difference in 30-day, 60-day or ICU mortality
- Significantly more in-hospital morbidity
- Increased in organ dysfunction
- More frequent cardiac complications in the liberal-strategy group
- Less transfusions given

CRIT Study

- 284 ICUs in 213 American Hospitals
- 4892 patients enrolled
- Prospective observational study
  - No change in transfusion practice
  - Patients who received blood
    - More complications
    - Higher mortality
    - Longer LOS

Corwin. Crit Care Med, 2004

**Decrease in Transfusion**

Maintaining a hemoglobin concentration from 7-9 g/dL decreased the average PRBC transfusion rate by 54%

- IOM
- ASA
- ACCP
- SCCM

**Why Take The Risk??**

- Does a blood transfusion increase oxygen delivery?
- Does a blood transfusion increase oxygen consumption?
- Why do people need transfusions

**Compensation for Reduced Oxygen Carrying Capacity**

- Increased cardiac output
- Increased oxygen extraction
- Shift of oxyhemoglobin dissociation curve

![Oxyhemoglobin dissociation curve](image-url)
RBC Storage

- Storage >15 days
  What happens to the RBC when it is stored?
  - Decreased ability to deform and unload oxygen in the microcirculation
  - Complete depletion of 2,3-diphosphoglycerate concentrations reducing the ability to offload oxygen by >50%
- 20% of all RBCs transfused in the United States are >28 days old

Risk of Transfusions

- Age of blood and the “storage lesion”
  - Increased nosocomial infections in critically ill patients
  - Nahra R et al retrospectively reviewed transfused pts in an ICU and nosocomial infections
    - Blood stored ≥ 29 days associated with higher nosocomial infections (OR 2.1 [1.2-3.0], p=0.01)
    - Higher number of units (≥ 5) associated with at least one infection (p=0.042)
    - No significant association with mortality

RBC Shape

- RBC ATP levels decrease during storage
  - RBC becomes a sphere instead of a disk
  - Loss of membrane lipid
  - Decrease in cellular deformability
  - Capillary sludging and obstruction predisposing to tissue ischemia and decreased oxygen delivery

Antioxidants

- Loss of antioxidants during storage
  - Increases oxidative injury resulting in the conversion of hemoglobin to methemoglobin

Clinical Outcomes With Increased Storage Duration

- Increased length of stay in the hospital and the ICU
- Increased multiple system organ failure
- Increased infections
- Impaired tissue oxygen utilization

SDF- sidestream dark field imaging is based on light absorption by hemoglobin in RBCs. It allows measurements that could be extrapolated into microcirculation flow

NIRS - near infrared spectroscopy - provides measurements of tissue O2 saturation and tissue hemoglobin index

Studies to See About Oxygenation Impact with Transfusions
Some Evidence

The effect of RBC transfusion on tissue oxygenation and microcirculation in severely septic patients.

Prospective observational study of 21 patients:

Patients were transfused for Hg <7, or for Hg between 7 and 9 with lactic acidosis, and SvO2 <70%.

NIRS and SDF-derived measurements of microcirculation and peripheral tissue oxygenation were obtained immediately before and 1 hr. after transfusion of 1 U RBC, stored up to 42 days, none were leukoreduced.


Results

Despite all 21 patients showed increase in Hg by more than 1g/dL there was NO effect of RBC transfusion on NIRS-derived variables. However there was an improvement in O2 consumption in pts with low baseline O2 consumption and deterioration in O2 consumption in pts with normal baseline.

When OLD is TOO Old?

RBCs are stored up to 42 days under temperature 1-4C with additive solutions. In some centers it is 35 days- both in the US and abroad.

Storage may decrease risk of developing some viral infections, Graft vs Host dx and some bacteria and parasites that do not survive under these temperatures.

The question remains of the effectiveness of oxygen carrying capacity

Question of Leukoreduction.

- **Synonyms**: leukodepletion, filtered (platelets), leuko-poor, buffy-coat reduced.
- **Purpose**: reduction of antigens presented by leukocytes with decrease of immune reactions to product (TRIM)
- **Benefits**: reduction in TRALI and TACO, decrease in febrile non-hemolytic transfusion reactions, HLA alloimmunization, minimizing of transmission of leukotropic viruses (EBV, CMV)
- **Negative effects**: cost related. Mostly not used in the US.

What About Artificial Blood?

- O2 carrying capacity
- Long shelf life
- Minimal reactivity
- No disease transfer
- Reasonable cost
- No immune impact
- ???Polyheme ...the answer to everyone’s dream????

NOT

Give Them Their Blood!
Limit Need for Transfusion when Possible: Preoperative Strategies

- Assessment of anemia
- Assessment of bleeding risk
- Preoperative recombinant human erythropoietin (rHuEPO) and iron (Fe+)

Preoperative Assessment

- History
  - Bleeding, previous operations, comorbidities, medications, anemias
  - Identify risk factors for transfusion
    - Aspirin
    - Coumadin
    - Lovenox®
    - Celebrex®
    - Plavix®
    - NOACs
    - Vitamin E/C/B
    - Gingko supplements
    - Garlic
    - Saw Palmetto
    - Alcohol
    - OTC meds/herbs/supplements

Prevalence of Anemia – Surgical Patients

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>Study</th>
<th>N</th>
<th>Prevalence of Anemia (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip and knee replacements only</td>
<td>Gruson et al (2008)</td>
<td>395</td>
<td>45.6</td>
</tr>
<tr>
<td>Myers et al (1991)</td>
<td>27,370</td>
<td>10.8</td>
<td></td>
</tr>
<tr>
<td>Bonnet et al (1997)</td>
<td>90</td>
<td>41.1</td>
<td></td>
</tr>
<tr>
<td>Tjalhamas et al (1992)</td>
<td>204</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>General ortho (Hip/knee + other)</td>
<td>Goodnough et al (1994)</td>
<td>265</td>
<td>25</td>
</tr>
<tr>
<td>Noncardiac</td>
<td>Dunne et al (2011)</td>
<td>6301</td>
<td>33.9</td>
</tr>
<tr>
<td>Colorectal</td>
<td>M’Koma et al (1994)</td>
<td>32</td>
<td>22</td>
</tr>
<tr>
<td>Cappell, Goldberg (1992)</td>
<td>315</td>
<td>Dukes A: 39.1 Dukes B &amp; C: 56.8 Dukes D: 75.8</td>
<td></td>
</tr>
</tbody>
</table>

Surgical Blood Loss - Gynecologic Surgery

<table>
<thead>
<tr>
<th>Surgical Procedure</th>
<th>Estimated Blood Loss (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal hysterectomy</td>
<td>500 - 800</td>
</tr>
<tr>
<td>Radical hysterectomy, cervical carcinoma</td>
<td>1250 - 1700</td>
</tr>
<tr>
<td>Vaginal hysterectomy</td>
<td>200 - 460</td>
</tr>
<tr>
<td>Laparoscopic vaginal (LAV) hysterectomy</td>
<td>240-275</td>
</tr>
</tbody>
</table>

Erythropoietin Dosing (Pre-operative)

- Beginning 3 weeks pre-op
  - 600u/kg x 4 doses (T-21, T-14, T-7, DOS)
  - ~$2100
- Beginning 9 days pre-op
  - 300u/kg daily x 14 days, 9 preop + DOS + 4 postop
  - ~$4200
- Various iron regimen

Intraoperative Strategies to Avoid Transfusion

- Minimize intraoperative blood loss
- Preoperative autologous donation (PAD)
- Intraoperative blood salvage
- Acute normovolemic hemodilution (ANH)
**Preoperative Autologous Donation**

- 1 unit (10 ml/kg) collected per week preoperatively
- Hgb ≥ 11 g/dL
- Less stringent criteria than for allogeneic donor
  - Generally preclude positive viral markers, eg hepatitis B or HIV
- May be combined with preoperative rHuEPO
- American Association of Blood Bankers prohibits using any intended autologous blood for allogeneic transfusion


**Preoperative Autologous Donation**

- Contraindications
  - Evidence of infection or risk of bacteremia
  - Scheduled surgery to correct aortic stenosis
  - Unstable angina
  - Active seizure disorder
  - MI or CVA within 6 months
  - High-grade left main CAD
  - Cyanotic heart disease


**Autologous Blood Wastage**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>% Autologous Units Discarded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Knee</td>
<td></td>
</tr>
<tr>
<td>Revision Knee</td>
<td></td>
</tr>
<tr>
<td>Bilateral Knee</td>
<td></td>
</tr>
<tr>
<td>Primary Hip</td>
<td></td>
</tr>
<tr>
<td>Revision Hip</td>
<td></td>
</tr>
</tbody>
</table>


**Perioperative Alternatives: Preoperative Autologous Donation**

- Costly – procurement and discard
- Labor intensive – collection and storage
- Inconvenient for patients
- Poor efficacy – $1 million/patient life year saved
- Transfusion:Donation ratio – 1:2 adds to cost

**Intraoperative Blood Salvage**

- CellSaver 5 System® (Haemonetics, Braintree, MA)
  - Double-lumen aspiration (suction) tubing, with infusion of acid citrate dextrose (ACD) anticoagulant
  - Passed through 150 μm filter into centrifuge bowl
  - Washed with 0.9% normal saline
  - Centrifuged and transfused

Intraoperative Blood Salvage

- Cost is for disposables (tubing, filter, centrifuge bowl), machine maintenance, and perfusionist
  - $197 + perfusionist
- Allogeneic unit RBCs $469
- Phillips et al showed the cost-effectiveness of IBS when more than 2 units allogeneic RBCs

Intraoperative Blood Salvage

- Generally contraindicated in patients with cancer, infection and the presence of enteric or amniotic fluid
- Should not be used with local blood clotting agents: fibrin glue, thrombin, collagen hemostatic material

Acute Normovolemic Hemodilution

- Before or just after the induction of anesthesia, blood is removed and stored in the operating room
- Intravascular volume is maintained with colloid infusion
- Hematocrit is diluted to 18-30% prior to incision
- At the end of the procedure, the patient’s blood is reinfused

Acute Normovolemic Hemodilution

- Preserved RBC 2,3-DPG level
- Whole blood returned (contains platelets and clotting factors)
- Inexpensive, relatively safe
- May be acceptable to Jehovah’s Witnesses

Peri-Op Autologous Donation v. Acute Normovolemic Hemodilution

<table>
<thead>
<tr>
<th></th>
<th>PAD</th>
<th>ANH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptable to JW pts</td>
<td>No</td>
<td>Yes*</td>
</tr>
<tr>
<td>ABO Mismatch</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Inconvenient/Expensive</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Plasma/Platelets wasted</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Decrease 2,3-DPG level</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Blood Wastage</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

The Military Experience

- In forward operating bases, blood storage is not available
- The “walking blood bank”
- Transfusion of whole, fresh blood for early resuscitation of showed improved outcomes

Crystalloid 3:1 Ratio

Blood 6-10 u PRBC
FFP Crystalloid
The Military Experience

- Adopting to civilian trauma centers
- In lieu of whole, fresh blood, simulate with “high ratio” transfusion
  
  1:1:1
  PRBC:plasma:platelets
  
- Massive transfusion protocols (MTP)

Massive transfusion

- ≥10 RBC units transfused in 24 hours
- Defines a group of injured patients with
  - 50% mortality
  - Hypothermia
  - Coagulopathy
  - Acid-base disturbances
  - Electrolyte derangements
  - Increased risk for ARDS

Therapeutic Anticoagulation

- Warfarin (Coumadin)
  - first used as a rodenticide in 1948
  - approved for human use as an oral anticoagulant in 1956
  - Vitamin K a known antidote since development
  - Rapidly? corrected with plasma transfusion

- Novel oral anticoagulants (NOAC’s)
  - Expanding indications and usage
  - Does not require frequent blood tests
    - dabigatran (Pradaxa) – approved 2010
    - rivaroxaban (Xarelto) – 2011
    - apixaban (Eliquis) – 2012
    - Edoxaban (Savaysa)
    - others...

- Novel oral anticoagulants (NOAC’s)
  - Until recently, no reversal agents
  - Now with idarucizumab (Praxbind), a monoclonal antibody to reverse dabigatran (Pradaxa)
    - Approved in 2015
  - Andexanet alfa 2018
  - More reversal agents in development !!!!!
Adjuncts in Transfusion

Thromboelastography (TEG) or rotational thrombelastogram (ROTEM)
- Core lab or near-patient testing
- Assessment of different pathways in clot formation and fibrinolysis

Adjuncts to Transfusion

- Tranexamic acid (TXA) in trauma
  - Antifibrinolytic, relatively cheap, available
  - CRASH-2 trial
    - Multicenter, multinational, randomized, placebo-controlled trial of TXA in trauma
    - Approximately 10,000 patients in each arm
    - Small but statistically significant mortality decrease
      - All cause mortality (16.0 v 14.5%)
      - Bleeding related mortality (5.7 v 4.9%)
    - U.S. studies ongoing


Indications for Blood Transfusions

- 60-70% transfused in the perioperative period
- ASA guidelines recommend maintaining perioperative Hgb levels higher than 6-8 g/dL
- National Institute of Health considers a Hgb >7 g/dL
- Special consideration and lower transfusion threshold may be required in patients aged>80 yr, those with CAD, fever and hypermetabolic states
- Patients with CAD, the cardiac compensatory mechanisms of dilutional anemia are still preserved at Hgb of 10g/dL even when receiving chronic beta blockade
- Whether patients with acute coronary syndromes may benefit from higher Hgb concentrations (11-12g/dL) is debatable

Indications for Blood Transfusions

- Platelet transfusion usually indicated when counts are <50,000 or platelet dysfunction is suspected (microvascular bleeding)
- FFP transfusion is based on obtained coagulation tests, presence of microvascular bleeding (massive blood transfusion), warfarin reversal and treatment of ATIII deficiency
- Cryoprecipitate administration is rarely indicated if serum fibrinogen level >150 mg/dL (unless there is microvascular bleeding or congenital deficiency)
- Despite these set guidelines, the transfusion practice still remains too and inconsistent with the evidence

Jehovah’s Witnesses

- Founded in 1872 by Charles Taze Russell in Pennsylvania
- Original name “Zion’s Watch Tower Tract Society” with Watchtower Magazine Publications
- In 1931, new president Joseph Franklin Rutherford, changed name to “Jehovah’s Witnesses” based on Isaiah 43:10-12
- 8 million members worldwide with international headquarters in Brooklyn, NY
- Hierarchical structure with group of elders who establish all doctrines based on their interpretations of the Bible.
**Jehovah’s Witnesses Doctrines**

- House to house visits with literature distribution and member recruitment is a requirement
- Baptism as an adult only
- No long hair or beards, emphasis on grooming
- Gambling, tobacco and illicit drugs are forbidden while drinking alcohol is permitted in moderation
- JW refuse to vote, salute the flag, all of which considered sign of paganism
- Do not celebrate holidays (birthdays, Christmas, Easter)
- Do not serve in armed forces
- **Refuse blood transfusion**

**Basis for Blood Refusal**

- Violation of God’s law and based on Biblical directive to “abstain from blood” Acts 15:29, even in “a life or death” situations.
- Grounds for expulsion from the religion, “the life of all flesh is the blood thereof: whoever eat it shall be cut off” Leviticus 17:10-16
- No whole blood and its components (RBC, WBC, platelets and plasma)
- No preoperative autologous blood collection and storage for later use (blood must remain in continuum with the body)

**Acceptable Alternatives**

- Based on personal choice
- Derivatives of blood components: albumin, cryoprecipitate, clotting factor concentrates (fibrinogen concentrate), prothrombin complex concentrate, DDAVP, recombinant Factor VII and immunoglobulins.
- Many JW may not object to intraoperative cell salvage, apheresis, hemodialysis, cardiac bypass, normovolemic hemodilution as long as the equipment is primed with non-blood fluids and blood remains in the continuum with body

**Case Presentation**

JH is a 4 yo boy who was brought to ED by parents with concern of intermittent vomiting and gait changes
- **PMHx:** Asthma and Eczema
- **PSHx:** none
- **Allergies:** Shellfish
- **PE:** Asymmetrical smile with minimal right sided facial droop
- **CT head w/o contrast:** 5x5 cm mixed cystic solid left cerebellar mass and obstructive hydrocephalus. Basal cistern compression and crowding of the foramen magnum. Probable pilocytic astrocytoma.

**Case Presentation: Hospital Course**

- PICU admission with Neurosurgery consult
- Elective intubation at bedside for EVD placement
- Pt remained intubated and sedated in anticipation of 2 stage surgery
- PICU and Neurosurgical residents obtained surgical consents but no blood consent due family’s refusal for blood transfusion
Case Presentation: Hospital Course

- On the morning of surgery case is postponed due to lack of consensus on blood transfusion.
- After about 12 hrs of conferences and ethics consult, family agreed to sign the consent for blood transfusion in the event of a life-threatening emergency only.
- Pt underwent stage 1: Suboccipital craniectomy, stereotactic cyst fenestration w/o complications (starting Hgb was 10.3 and recorded intra-op EBL of ~10cc).
- Two days later pt underwent stage 2: Tumor resection w/o need for blood transfusion (EBL of 100cc and post-op Hgb of 9.5).
- Surgical pathology confirmed pilocystic astrocytoma WHO grade I.
- Extubated on POD2, EVD removed on POD 5.
- On HD 15, pt discharged home in stable condition on ferrous sulfate and dexamethasone.

Legal Considerations

- Legally, except in an emergency, parental consent is necessary to perform any medical procedure on a child.
- Two arguments commonly used by parents when they refute treatment are parental rights to raise children as they see fit and religious freedom.
- Courts throughout the western world recognize parental rights, but these rights are not absolute.

“Helpless Acceptance”

- When seeking parental consent, keep in mind:
  - Many parents are aware of surgical risks and accept the possibility of blood transfusion but due to religious restraints unable openly express their wishes.
  - Avoid judgment and acknowledge the difficulty of situation.
  - Keep language simple and compassionate.
  
  "As JW, our religious beliefs do not support the use of blood transfusions. We have made our beliefs clear to the care team and they are aware that blood transfusions should be avoided. We are confident that the care team understands our position. We absolutely want the best for our son. We want to proceed with surgery and want the care team to do all that is necessary to save his life and ensure the best outcome for him."
  
  - Speak to them alone (39% agreed).
  
  - Disfellowshipping.

Better to Be Good then Lucky!

- Cases reports indicate that survival with preserved organ function is possible in patients with Hg as low as 3g/dL.
- Published record belongs to 53 y.o. victim of stab wounds who survived Hg 0.7 gm/dL (Hct 2.2%) without any transfusion (Anesthesia Analgesia 2010).
**Human Error in Blood Transfusions**

- Human error is a persisting problem for blood transfusion.
- It is 100 times more common than transmission of HIV.
- 50% of all blood units are estimated to be transfused by anesthesia personnel.
- Over half of all fatalities from BT are attributed to preventable errors.
- Risk of error 1:12,000-19,000
- Risk of fatal outcome 1:600,000-800,000
- In the US aggregated risk of all transmissible infections is less than half of the risk of transfusion error.
- Each anesthesiologist estimated to administer wrong blood to a patient at least once in a lifetime.

Clifford, et al J of Invest Med 2017

**In some countries (Germany) the whole process of blood handling is subject to very strict regulations by government. Bedside pre-transfusion compatibility testing remains mandatory, done by physician in person.**

In San Rafael Hospital, Milan, Italy there is pilot program that greatly reduces errors- RFID.

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**Final Thoughts**

- Multiple RCTs and recent meta-analysis of 19 trials (total of 3647 patients) support the use of restrictive transfusion strategies.
- Publication from The International Consensus Conference on Transfusion Outcomes (2016) that encompassed 494 studies stated that 88% of allogeneic BT were inappropriate.
- The Joint Commission, the AMA and Centers for Medicare/Medicaid Services joined to identified RBC transfusions as 1 of the top 5 overused procedures in medicine.

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**Conclusions**

- Anemia happens to patients
- Transfuse the bleeding patient
- Those who are not bleeding, consider the risks....they likely will not do better with the transfusion and may do worse
- We need to do better at selecting patients to transfuse based on evidence