Optimal Use of Blood Component

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Blood Components

- PRCs: leukocyte-depleted
- Platelets:
  - Platelet concentrate
  - LPPC (leukocyte-poor platelet concentrate)
  - SDP (single donor platelet)
- Fresh frozen plasma (FFP) with or without cryoprecipitate
- Cryoprecipitate
- Fresh whole blood
Adverse Effects Associated with Allogeneic RBC Transfusion: Infectious

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>Incidence per transfused units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>1:2,000,000</td>
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<tr>
<td>Hepatitis B</td>
<td>1:31,000 - 1:81,000</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1:1,935,000 - 1:3,100,000</td>
</tr>
<tr>
<td>HIV</td>
<td>1:2,135,000 – 1:4,700,000</td>
</tr>
<tr>
<td>HTLV I/II</td>
<td>1:1,900,000</td>
</tr>
<tr>
<td>Bacterial contamination</td>
<td>1:14,000 – 1:28,000</td>
</tr>
<tr>
<td>Parasitic infection</td>
<td>1:4,000,000</td>
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<tr>
<td>Prion disease</td>
<td>rare</td>
</tr>
</tbody>
</table>


Adverse Effects Associated with Allogeneic RBC Transfusion: Noninfectious

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>Incidence per transfused units</th>
</tr>
</thead>
<tbody>
<tr>
<td>• FNHTR</td>
<td>1:500</td>
</tr>
<tr>
<td>• Urticarial reaction</td>
<td>1:50-1:100</td>
</tr>
<tr>
<td>• Anaphylactic reaction</td>
<td>1:23,000</td>
</tr>
<tr>
<td>• HTR</td>
<td>1:9,000</td>
</tr>
<tr>
<td>• TRALI</td>
<td>1:1,300-1:5,000</td>
</tr>
<tr>
<td>• TACO</td>
<td>1:17,000</td>
</tr>
<tr>
<td>• Post-transfusion purpura</td>
<td>1:143,000</td>
</tr>
</tbody>
</table>
PRCs

• Shelf-life 21-42 days
  – ACD/CPD/CP2D 21 days
  – CPDA-1 35 days
  – Additive solution 42 days
  – Open system 24 hours
• Volume 250-350 mL
• Red cells 65-80%
• Plasma 20-35%
• Typical dose 2 units or 15 mL/kg
• Raises Hb ~ 2 g/dL
Indications for PRCs Tx

• Acute blood loss with impaired $O_2$ delivery
  – threshold for PRCs Tx: Hb < 6 g/dL
  – Class II hemorrhage ~ 15-30% blood volume loss (1500 mL): young healthy pts can tolerate with crystalloid
  – Class III hemorrhage % ~ 30-40% loss: need Tx

• Anemia: chronic anemia is better tolerated than acute anemia
**Platelets (Random donor platelet concentrate)**

- Shelf-life 5 days
- Volume 50-60 mL
- Platelets $7.5 \times 10^{10}$
- Typical dose 6 units or 5 mL/kg
- Raises platelet count $\sim 50 \times 10^{9}$/L
Platelets (Apheresis collected single donor platelet concentrate)

- Shelf-life 5 days
- Volume 250-300 mL
- Platelets 3-6 x 10^{11}
- Typical dose 1 unit
- Raises platelet count ~ 50 x 10^9/L
Indications for Platelet Tx (1)

- Platelet count < 10 $\times 10^9$/L, asymptomatic
- Platelet count < 15 $\times 10^9$/L with a coagulation disorder or minor bleeding
- Platelet count < 20 $\times 10^9$/L with major bleeding
Indications for Platelet Tx (2)

- Platelet count < 50 x10⁹/L with an invasive procedure (thoracentesis, paracentesis) or general Sx required or during massive Tx (1-2 blood volumes)
- Platelet count < 100 x10⁹/L with neurologic or cardiac Sx
FFP

- Shelf-life 1 year (frozen) and 24 hours after thawed
- Volume 200-250 mL
- Coagulation factor 200-250 units and fibrinogen 400-500 mg
- Typical dose 4 bags or 15 mL/kg
- Raises most coagulation factors levels ~ 20%
Indications for FFP Tx

- Rapid reversal of warfarin overdose
- Bleeding and multiple coagulation defects as evidenced by $\uparrow$ PT/INR/aPTT $> 1.5$ control (liver disease, DIC)
- Correction of coagulation defects for which no specific factor is available
- Tx $> 1$ blood volume with evidence of active bleeding and $\uparrow$ PT/INR/aPTT
- TTP, antithrombin deficiency, hereditary angioedema
Cryoprecipitate

- Shelf-life 1 year frozen
- Volume 20-50 mL
- Factor VIII 80-100 units, fibrinogen 225 mg, and vWF variable amounts
- Typical dose 10 bags or 1 bag/5 kg
- Raises fibrinogen 75 mg/dL
Indications for Cryoprecipitate Tx

- **Bleeding in hemophilia A**
  - 1 unit/kg → raises F VIII 2%
  - 1 bag cryoprecipitate → F VIII 100 unit

- **Bleeding in vWD that are unresponsive to desmopressin (DDAVP)**

- **Bleeding conditions with fibrinogen < 100 mg/dL**
Bleeding in Hemophilia A
Massive Transfusion

• Replacement of one blood volume or ~ 10 units of PRCs within a 24-h period
• < one blood volume: rarely need FFP or platelet replacement
• Two blood volume or > 20 units PRCs should transfuse FFP and platelet
• 1-2 blood volume should transfuse if:
  – Platelet < 50 x 10⁹/L → platelet Tx
  – INR > 1.5 → FFP Tx
  – Fibrinogen < 100 mg/dL → cryoprecipitate Tx
Optimal Use of Blood Component

- Use as indications
  - According to signs & symptoms, not just by lab directed
  - Use as minimal as possible
- Consider drugs in stead of blood component if possible
- Preoperative autologous transfusion
- Perioperative collection
Preoperative Autologous Donation

- **Short-term storage: within 28-42 days**
  - Non ER surgery
  - Expected blood loss during surgery: orthopedics, intra abdominal eg. hysterectomy
  - Prepare when surgery is planned
  - No. of unit needed: 2 units: 2 weeks, 3 units: 3 weeks

- **Long-term storage: 7-10 years**
Preoperative Autologous Donation: Contraindications (1)

- IHD with angina at rest
- Acute MI within 3 months
- CHF
- Aortic stenosis
- Ventricular arrhythmia
- Cerebrovascular disease with TIA
- Severe HTN
Preoperative Autologous Donation: Contraindications (2)

- Having infection or septicemia during collection eg. post dental extraction, post sigmoidoscopy, post barium enema
- Experience fainting after previous donation
- Hct < 33% before collection
Preoperative Autologous Donation

Ferrous sulfate
Anemia ≠ PRC 2 units
Anemia

- Is very common in medical patients
- > 50% of patients admitted to medical ward are anemic
- Is only clinical manifestation of many diseases both benign and malignant
- Rx is not just blood transfusion, FBC or folic acid
Pathophysiology of Anemia

• Decreased production
  – AA, acute leukemia, PRCA, CKD, myelophthisic anemia, ACD

• Increased destruction
  – AIHA, thalassemia, G-6PD def, hypersplenism, PNH, hemophagocytic syndrome

• Ineffective erythropoiesis
  – Megaloblastic anemia, MDS
Drugs

- Nutritional anemia: iron, vit B12, folate instead of PRCs Tx
- AIHA: use corticosteroids first
- ACD: EPO
- MDS: EPO + G-CSF
- Bleeding
Nutritional Anemia

• Iron Deficiency: Ferrous sulfate 1 x 3 PO ac x 6-12 months with correction of blood loss

• Pernicious anemia or post gastrectomy: vit B$_{12}$ IV/IM OD x 7 days → weekly x 4 → monthly indefinitely

• Hemolytic anemia (thalassemia, HS, AIHA): folic acid (5 mg) 1 x 1
FBC (Ranbaxy Unichem)

- Fe fumarate: 200 mg
- Vitamin B1: 2 mg
- Vitamin B2: 2 mg
- Vitamin B12: 5 μg
- Vitamin C: 20 mg
- Niacin: 10 mg
- Folic acid: 100 μg
- Ca phosphate tribasic: 100 mg
AIHA: Management

- $O_2$, bed rest
- Corticosteroids
- RBCs Transfusion
- Other Rx: high dose steroids, IVIg, splenectomy, immunosuppressive agents, CSA, MMF, danazol, rituximab, HSCT
## Guidelines for RBCs Tx in AIHA

<table>
<thead>
<tr>
<th>Average Hb (gm/dl)</th>
<th>Probability of significant impairment</th>
<th>Transfusion strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 10</td>
<td>very low</td>
<td>avoid</td>
</tr>
<tr>
<td>8-10</td>
<td>low</td>
<td>avoid</td>
</tr>
<tr>
<td>6-8</td>
<td>moderate</td>
<td>try to avoid; Tx if possible</td>
</tr>
<tr>
<td>≤ 6</td>
<td>high</td>
<td>required</td>
</tr>
</tbody>
</table>

Petz LD. Clinical Practice of Transfusion Medicine 1996
RBCs Transfusion in AIHA (1)

- Use new unit of blood and a least incompatible unit
- In fulminant hemolysis, Tx incompatible blood before completion of the evaluation may be imperative and life-saving
- Should give corticosteroid first
RBCs Transfusion in AIHA (2)

- If possible, use leukocyte-reduced RBCs to avoid a possible febrile transfusion reaction that might be confused with a hemolytic reaction
- Use smallest volume and prolonged transfusion
Bleeding (1)

- **Warfarin**: vit K1
- **Heparin**: protamine 1 mg ~ 100 units UFH
- **Obstructive jaundice**: vit K1
- **Prolonged NPO + TPN or antibiotics**: vit K1
- **Mild hemophilia A**: DDAVP (desmopressin)
Bleeding (2)

- Hemophilia with inhibitor: recombinant activated factor VII
- Uremia: DDAVP, EPO, cryoprecipitate
- ITP: corticosteroids
- Cardiovascular Sx (CPB): antifibrinolytics eg. tranexamic acid, aprotinin
- Viper bite: antivenoms
Aminocaproic acid
Tranexamic acid
งกะปะ (Calloselasma rhodostoma)

พิษงูมี thrombin like activity ทำให้เกิด Hypofibrinogenemia Compartment syndrome

เป็นงูที่ขนาดตัวไม่ใหญ่ หัวของมันเป็นรูปสามเหลี่ยมคอดเล็ก ลำตัวสีน้ำตาล แดง มีลายรูปสี่เหลี่ยมขนมปูนสีน้ำตาลเข้ม ตามข้างลำตัว แนวกระดูกสันหลังนูนเป็นสันขอบขัดตัว นอนนิ่งๆ อยู่ใต้กองใบไม้ หรือในพงหญ้าที่รกๆ ตามกองหิน ชอบเคลื่อนไหว แต่สามารถพุ่งกระโดดได้รวดเร็ว พบได้ทุกภาคของประเทศไทย แต่จะชุกชุมทางภาคใต้
งูแมวเซา (Vipera russelli siamensis)

พิษงูกระตุ๊น Factor X ทำให้เกิด DIC ARF

เป็นงูที่มีลำตัวอวันสั้น หัวค่อนข้างเป็นรูปสามเหลี่ยม บนหัวมีแต่เกล็ดเล็ก ๆ ปกคลุมอยู่ ไม่มีเกล็ดแผ่นใหญ่เลย สีตัวเป็นสีน้ำตาลอ่อน มีลายสีน้ำตาลเข้ม ๆ เป็นดวงกลม ๆ ตามตัว มีนิสัยดุร้าย เวลาถูกกระตุ๊น สามารถพ่นพื้นหมดออกมาทางรูจมูก เกิดเป็นเสียงขูดดังกลัวได้ ฉกกัดศัตรูได้รวดเร็ว งูแมวเซามีชุกชุมทางภาคกลาง
Indications for Viper Antivenom

- Systemic bleeding
- VCT > 30 min.
- Severe thrombocytopenia < 20-30 x 10^9/L
- Impending compartment syndrome
Warfarin Overdose
D/C Warfarin

- INR < 5 without clinically evident bleeding
  - Observation with serial PT/INR
- INR 5-9 and no significant bleeding
  - Oral vit K₁ 1-2.5 mg if pt at increased bleeding risk
- INR > 9 and no significant bleeding
  - Oral vit K₁ 3-5 mg
- INR > 20 or clinically significant bleeding
  - FFP 10-15 mL/kg or vit K₁ 10 mg IV slowly
Heparin Overdose

• Minor bleeding
  – Observation with serial aPTT

• Major bleeding
  – Protamine 1 mg per 100 units of heparin IV slowly
  – Protamine will neutralize the antithrombin effect of LMWH but incompletely reverses factor Xa inhibition (1 mg: 1 mg of enoxaparin and 100 units of dalteparin)
  – FFP and/or PRC in life-threatening bleeding
Jehovah’s Witnesses in Thailand

- ~2,000-3,000
- Refusal any blood component transfusion even their own blood → autotransfusion
- Accepted Rx: EPO, antifibrinolytic, rFVIIa, IVlg
Jehovah’s Witness
In Thailand

Phuket Meeting
5-8 October 2007
1. Initiation phase

Injury of vessels wall leads to contact between blood and subendothelial cells.

Tissue factor (TF) is exposed and binds to FVIIa or FVII which is subsequently converted to FVIIa.

The complex between TF and FVIIa activates FIX and FX.

FXa binds to FVa on the cell surface.
2. Amplification phase

The FXa/FVa complex converts small amounts of prothrombin into thrombin.

The small amount of thrombin generated activates FVIII, FV, FXI and platelets locally. FXIa converts FIX to FIXa.

Activated platelets bind FVa, FVIIIa and FIXa.
3. Propagation phase

The FVIIIa/FIXa complex activates FX on the surfaces of activated platelets.

FXa in association with FVa converts large amounts of prothrombin into thrombin creating a “thrombin burst”.

The “thrombin burst” leads to the formation of a stable fibrin clot.
Tissue factor (TF)/FVIIa, or TF/rFVIIa interaction, is necessary to initiate haemostasis.

At pharmacological concentrations rFVIIa directly activates FX on the surface of locally activated platelets. This activation will initiate the "thrombin burst" independently of FVIII and FIX. This step is independent of TF.

The thrombin burst leads to the formation of a stable clot.
rFVIIa (Novoseven®)

- Is processed in cell cultures of baby hamster kidney cells
- When binding to tissue factor at the site of injury, it can activate F. X, IX and activated platelets causing fibrin plug
- Indications: severe bleeding and surgery in hemophiliac pts with inhibitors
- Others: severe liver diseases, platelet disorders
Digital ischemia after rFVIIa administration
ขอบพระคุณผู้ฟัง
Antithrombotic Drugs

• Warfarin: 2, 3, 5 mg tab
• Heparin: UFH, LMWH
• Antiplatelets: ASA, ticlopidine, clopidogrel
• Fibrinolytic drugs: streptokinase, urokinase, tPA
• Direct thrombin inhibitors: hirudin & analogues eg. Ximelagatran
• Pentasaccharide: fondaparinux (inhibits Xa)