แพทย์เรียนรู้เกี่ยวกับ Transfusion Therapy ได้อย่างไร

CLINICAL GUIDELINE
KNOWLEDGE GAPS: Physician

EDUCATION AND ADMINISTRATION

Transfusion medicine in American undergraduate medical education

Julie K. Karp, Christine M. Weston, and Karen E. King

Karp JK et al. Transfusion 2011;51:2470-79
KNOWLEDGE GAPS: Physician

- Education on transfusion indications and risks in medical school is minimal
- Undergraduate medical education curriculum consists of **1-2 hrs** of didactic lecture for TM
- Physicians learn from their physician mentors, who learned from their physician mentors, who learned from their physician mentors, who learned from their physician mentors...
- Practice is often by Tradition...Not evidence-based

Karp JK et al. Transfusion 2011;51:2470-79
VARIATION IN TRANSFUSION PRACTICE

CABG Surgery (1st time CABG) – STS institutions
• RBC Transfusion Rate = 10-90%
• FFP Transfusion Rate = 0-95%
• Platelet Transfusion Rate = 0-90%

Orthopedic Surgery (Total hip arthroplasty)
• RBC Transfusion Rate = 7-71%

Knowledge gap exists for best practice & appropriate blood use

Bennett-Guerrero E ;JAMA 2010;304(14):1568-75
OVERUTILIZATION

• Risk of Adverse Event  ความเสี่ยงต่อการเกิดปฏิกิริยา
• Unnecessary Cost  ค่าใช้จ่ายที่สูงขึ้น โดยไม่จำเป็น
• Blood Availability for those who need it  ไม่มีเลือดเหลือที่จะให้แก่ผู้ป่วยที่จำเป็นจริงๆ
The Appropriate Use of Blood and Blood Components
Physician Handbook
1st edition 2011
Replacement Therapy

- Replace when there is an evidence / clinical of deficiency
- ปัญหาเลือดออกของผู้ป่วย ไม่ได้เกิดจากการขาดส่วนประกอบของ เลือดเสมอไป

<table>
<thead>
<tr>
<th>Blood products</th>
<th>Indication for replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red cell products</td>
<td>Anemia, blood loss</td>
</tr>
<tr>
<td>Fresh frozen plasma</td>
<td>Coagulopathy</td>
</tr>
<tr>
<td>Platelet products</td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Cryoprecipitate AHF</td>
<td>Hemophilia A</td>
</tr>
</tbody>
</table>
Platelets are cytoplasmic fragments produced by megakaryocytes in the bone marrow. Platelets are classified as cells. Platelets are discoid in shape. Platelets do not have nucleus. Average life span: 10 days. 70% in circulation, 30% in spleen.
Platelet

- Gerüttelte Blut ist cellular components.
- Спираль плазмы может содержать red cell пленок бар.
- Сигналы синхронизации будут показывать swirling effect.

Normal platelets
WBD Platelet Products

(a) PRP Technique

Whole blood held at 22°C for up to 8 hrs

Soft spin 22°C

Leukoreduction filter

Leukoreduced platelet-rich plasma

Hard spin 22°C

RBC

Plasma

Platelets

(b) Buffy Coat Technique

Whole blood held at 22°C for up to 24 hrs

Hard spin 22°C

Discarded waste

Pool & soft spin 22°C

Pooled leukoreduced platelets

RBC

Plasma

Buffy coat
Platelet pool from buffy coated method

Pool 4-6 BCs + 1 unit PPP

Soft spin

Pooled PC  waste

LPPC

Plasma/Red Cells Level

Buffy Coat

Platelet Poor Plasma

Buffy Coat Depleted Red Cell Concentrate

LPRC

FFP
Platelet content in each unit

- Platelet conc.
  - $7 \times 10^{10}$ / unit
  - $4.0 \times 10^{11}$ (pool 5 unit)

- Single Donor Platelet
  - $3.0 - 4.0 \times 10^{11}$

- LPPC
  - $3.5 \times 10^{11}$

Therapeutic doses
Basic requirements for Platelets storage

• Platelets should be stored at 22-24°C (controlled temperature): aging process slows down at 22-24°C as compared to 37°C

• Continuous gentle agitation must be maintained on a flat bed agitator

• pH should be above 6.2

• Plasma 50-60 mL is needed for storage

5 days storage
Continuous agitation

ไม่ควรนำไปเก็บในตู้เย็นที่ดูดซับน้ำ

เก็บได้นาน 5 วัน

22 -24 C
Continuous agitation

ตู้เก็บเกิดเลือด
Particulate Matter (clots) – Platelets
Not Acceptable for Transfusion
Clot due to bacterial contamination
Indications for Platelet Transfusions

Prevention and Treatment of hemorrhage patients

Thrombocytopenia or platelet function defects

Cause of thrombocytopenia should be established before a decision about platelet transfusion
Platelet transfusion: Indications

- Bone marrow failure
- Platelet function disorder
- Massive blood transfusion
- Cardiopulmonary bypass surgery
- Disseminated intravascular coagulation
Approximately 2.2 million platelet doses are transfused annually in the United States.
The 2009 National Blood Collection and Utilization Survey Report

Figure 4-1. Trends in platelet transfusion, 1997-2008.

2008
Apheresis 87%
Platelet Transfusion: Indications

• Prophylactic:
  – Transfusing hospitalized adult patients with a platelet count of $10 \times 10^9$ cells/L or less to reduce the risk for spontaneous bleeding
  – patients having elective central venous catheter placement with a platelet count less than $20 \times 10^9$ cells/L.
  – patients having elective diagnostic lumbar puncture with a platelet count less than $50 \times 10^9$ cells/L.
<table>
<thead>
<tr>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Committee for Standards in Haematology, 1992</td>
</tr>
<tr>
<td>College of American Pathologists, 1994</td>
</tr>
<tr>
<td>Consensus Conference, Royal College of Physicians, Edinburgh, 1998</td>
</tr>
<tr>
<td>American Society of Clinical Oncology, 2001</td>
</tr>
<tr>
<td>British Committee for Standards in Haematology, 2001</td>
</tr>
<tr>
<td>Italian Society of Transfusion Medicine and Immunohaematology, 2009</td>
</tr>
</tbody>
</table>

*Consider raised threshold for patients with additional risk factors for bleeding.

*Table 4: Medical society clinical practice guidelines for trigger for prophylactic platelet transfusions*
Platelet Transfusion: Indications

- patients having major elective non-neuraxial surgery with a platelet count less than $50 \times 10^9$ cells/L.

- surgeries involving the central nervous system, platelets are conventionally transfused prophylactically for a pre-procedure platelet count less than $80 \times 10^9$ to $100 \times 10^9$ cells/L,
ข้อควรรู้เกี่ยวกับเกร็ดเลือด

- เป็นทรัพยากรที่สำคัญ และมีจำนวนไม่เพียงพอ
- เมื่อพร้อมที่จะให้ จึงให้คนมารับที่ธนาคารเลือด เจ้าหน้าที่ธนาคารเลือดจะรวมหลายๆถุงเป็นถุงเดียว
- หลังจากรวมเป็นถุงเดียว ควรให้ภายใน 30 – 60 นาที
- ไม่ควรนำเข้าไปเก็บไว้ในตู้เย็นที่หอผู้ป่วย ขณะที่รอเริ่ม Transfusion
- ควรให้หมดภายใน 30 – 60 นาที
- อาจจะให้ไม่ตรง ABO ในกรณีที่ไม่มี
- ต้องใช้ชุดให้เลือด (Transfusion set) ตามปกติ ไม่ควรใช้ร่วมกับชุดที่ให้ เม็ดเลือดแดง
Poor Response to Platelet Transfusion

- Platelet factors
- Patient factors – nonimmune
  - Majority of cases
- Patient factors – immune
Patient Factors – Immune

- HLA class I alloimmunization (most common)
- Platelet-specific antigen alloimmunization
- ABH alloimmunization
- Autoantibodies
- Drug-related antibodies
Platelets stored in Platelet Additive Solution (PAS)
Primary ingredients

1. Citrate : To prevent activation of coagulation
2. Acetate : To serve as a substrate for oxidative metabolism
3. Sodium chloride : For isotonicity and osmotic strength
4. Phosphate : Stimulation of glycolysis and maintainance of physiologic pH
5. Magnesium / Potassium : Decreases platelet activation, improve morphology score and decrease lactate production
ADVANTAGES OF PAS

• Clinical advantages:
  – More Plasma for using in transfusion and fractionation
  – Standardize composition
  – Ability to control storage environment
  – Sterile, pathogen free
  – Decrease reactions by removal of plasma
    • Less protein, fewer allergic reactions,
    • Lower ABO antibody titer
    • possibly TRALI?
Fatal Shock after Transfusion of Platelets Contaminated by Staphylococcus aureus
Fatal Shock after Transfusion of Platelets Contaminated by Staphylococcus aureus:

• ผู้ชายอายุ 60 ปี ได้รับการวินิจฉัยเป็น multiple myeloma รับไว้ในโรงพยาบาลตัวยาอาการ pancytopenia และ pneumonia.
• ผู้ป่วยได้รับยา melphalan และ prednisone นาน 3 สัปดาห์ และมีภาวะ severe global hypo-gammaglobulinemia.
• Empiric antibacterial chemotherapy with ciprofloxacin and tazobactam-piperacillin led to clinical improvement.
Fatal Shock after Transfusion of Platelets Contaminated by Staphylococcus aureus:

• At admission, the WBC count was 1100 cells/mm³ (lymphocyte count, 730 cells/mm³; monocyte count, 110 cells/mm³), and the platelet count was 26,000 platelets/mm³.

• Leukocyte-reduced platelets were transfused after the patient experienced a mild episode of hemoptysis. The unit of platelets was obtained by apheresis from a single donor 4.5 days before use.
Fatal Shock after Transfusion of Platelets Contaminated by Staphylococcus aureus:

• 20 minutes after the beginning of the transfusion, the patient developed chills, diarrhea, vomiting, tachycardia, and cardiovascular collapse.

• The transfusion was stopped immediately, after a total volume of 100 mL had been infused.

• 4 hours later, the patient's temperature was 39.1°C, and severe hypotension, hypoxemia, and confusion occurred, necessitating intensive treatment.
Fatal Shock after Transfusion of Platelets Contaminated by Staphylococcus aureus:

• Gram staining of residual platelets from the transfusion bag revealed large numbers of gram-positive cocci in clusters. Cultures of samples of venous blood and residual platelets yielded S. aureus isolates.

• The platelet donor was a healthy male volunteer who had undergone apheresis on several occasions. Nasal swabs showed S. aureus carriage. The result of a culture of an antecubital fossa swab specimen was negative.
Bacterial contamination of platelets UHCMC Cleveland 1991-2011 N=75
<table>
<thead>
<tr>
<th>Group</th>
<th>Implicated bacteria</th>
<th>Septic transfusion reactions</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Number</td>
</tr>
<tr>
<td><strong>Staphylococcus spp.</strong></td>
<td>Coagulate-negative staphylococcus</td>
<td>37†</td>
</tr>
<tr>
<td></td>
<td><em>Staphylococcus aureus</em></td>
<td>13†</td>
</tr>
<tr>
<td></td>
<td><em>Staphylococcus intermedius</em></td>
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<tr>
<td><strong>Streptococcus spp.</strong></td>
<td><em>Streptococcus viridans group</em></td>
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<tr>
<td></td>
<td><em>Streptococcus mitis/oralis</em></td>
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<tr>
<td></td>
<td><em>Streptococcus alactolyticus</em></td>
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</tr>
<tr>
<td><strong>Enterobacter spp.</strong></td>
<td><em>Enterobacter aerogenes</em></td>
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<tr>
<td></td>
<td><em>Enterobacter cloacae</em></td>
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<tr>
<td><strong>Klebsiella spp.</strong></td>
<td><em>Klebsiella pneumoniae</em></td>
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<tr>
<td></td>
<td><em>Klebsiella oxytoca</em></td>
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<td><strong>Others</strong></td>
<td><em>Acinetobacter baumannii</em></td>
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<tr>
<td></td>
<td><em>Enterococcus faecalis</em></td>
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</tr>
<tr>
<td></td>
<td><em>Pseudomonas fluorescens</em></td>
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<tr>
<td></td>
<td><em>Bacillus spp.</em></td>
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</tr>
<tr>
<td></td>
<td><em>C. perfringens</em>‡</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>68</td>
</tr>
</tbody>
</table>

* All cases met the hemovigilance definition for definite or probable septic transfusion reactions, as previously described.\(^1,2\) Cases during various time periods (March 1, 2004-May 31, 2006, and December 1, 2006-July 31, 2008) were also included in prior publications.\(^1,2\) All of the components implicated in septic reactions were from donations with negative QC aerobic culture results before transfusion.

† Includes seven reported fatalities that involved coagulate-negative *Staphylococcus* (two cases) and *Staphylococcus aureus* (five cases).

‡ Index case described in this report.
PASSPORT Surveillance Cultures

• 4369 PC initially culture negative
  – Re-tested after day 7
  – 3 true positives: *S. aureus*, *S. epidermidis*, *S. veridans*

• Residual risk: 686 per million PC (1 in ~1500)

L. Dumont, BPAC, May 2008
สาเหตุการตาย จากการได้รับเลือด ในสหรัฐอเมริกา

<table>
<thead>
<tr>
<th>Year</th>
<th>TRALI</th>
<th>HTR-non ABO</th>
<th>HTR-ABO</th>
<th>Microbial infection</th>
<th>TACO</th>
<th>Anaphylaxis</th>
<th>Other</th>
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<tbody>
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<td>FY08</td>
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<td>7</td>
<td>10</td>
<td>7</td>
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<td>FY11</td>
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<td>FY12</td>
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<td>3</td>
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<td>8</td>
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</tr>
</tbody>
</table>
Transfusion-related deaths
2010 to 2016 n=115

TACO = Transfusion associated circulatory Overload
Avoiding unnecessary transfusion

• Important strategy for reducing risks

• Supported in national patient blood management guidelines

• Three principles of patient blood management
  – Optimise the patient’s blood levels before a surgical or medical intervention
  – Lose less blood throughout the patient’s treatment
  – Optimise recovery including tolerance of anaemia
THANK YOU!

V. CHONGKOLWATANA