Platelet Transfusion: Back to Basics

Johnathan Mack, MD MSc FRCPC
The Ottawa Hospital
University of Ottawa
Outline

• Role platelets play in hemostasis
• Modes of production of platelet concentrates
• Indications for platelet transfusion
• Situations in which platelet transfusion may be ineffective or harmful
• Factors associated with poor recovery and survival of platelets
Clot formation

- Vessel Wall Injury
- Platelet Adhesion
- Fibrin Formation

→

- Vessel Wall Contraction
- Platelet Aggregation

Clot formation
Primary clot formation: the platelet plug

- Platelet activation leads to:
  - Shape change
    - Negatively charged lipids flipped to outside surface of platelet
  - Granule release
    - Alpha granules
      - vWF, angiogenic factors, angiogenesis inhibitors
    - Dense granules
      - ATP, ADP, serotonin, calcium
  - Attraction and activation of other platelets
- Platelets aggregate and primary clot ("platelet plug") forms
Thrombin and Fibrin formation

- Negative platelet surface provides platform for clotting ‘cascade’ resulting ultimately in thrombin generation, conversion of fibrinogen to fibrin, and secondary clot formation
The clotting cascade
Platelet Plug Formation

ENDOTHELIUM

PLATELET ADHESION to injured vessel: vWF binds GPIb

GLA

PLATELET AGGREGATION
Fibrinogen binds GPIIb/IIIa

PLATELET PLUG FORMATION
Fibrinogen binds GPIIb/IIIa

EXPOSED SUBENDOTHELIUM
Modes of Production
Whole Blood Derived (WBD)
Apheresis platelet concentrates
**Platelet units**

**Pooled Platelets (WBD)**
- Volume 330-360 mL
- ~300 x 10^9 platelets
- Whole blood derived platelet concentrates from 4-6 donors are pooled to create an effective dose
- This led to platelets being called “6-pack” or “4-pack”

**Apheresis Platelets**
- Volume 230-250 mL
- ~370 x 10^9 platelets
- Apheresis platelet units do not need to be pooled
Indications for platelet transfusion

- Prophylactic
- Therapeutic
Prophylactic Platelet Transfusion

• Hypoproliferative thrombocytopenia with PLT < $10 \times 10^9$/L
  • TOPPS trial: platelet transfusion when <10 was not non-inferior to no prophylaxis
• Central line placement with PLT < $20 \times 10^9$/L
• Non-neuraxial surgery with PLT < $50 \times 10^9$/L
• Lumbar puncture with PLT < $50 \times 10^9$/L
• Neuraxial surgery with PLT < $100 \times 10^9$/L
A No-Prophylaxis Platelet-Transfusion Strategy for Hematologic Cancers

Brennan C. Kahan, M.Sc., Claire Dyer, B.N., Louise Choo, Ph.D., Lekha Bakrania, B.Sc.,
Charlotte Llewelyn, Ph.D., Timothy Littlewood, M.B., B.Ch., M.D., Richard Soutar, M.B., Ch.B., M.D.,
Derek Norfolk, F.R.C.P., F.R.C.Path., Adrian Copplestone, M.B., B.S., Neil Smith, M.B., Ch.B.,
Paul Kerr, M.B., Ch.B., Ph.D., Gail Jones, M.D., Kavita Raj, M.D., Ph.D., David A. Westerman, M.B., B.S.,
Jeffrey Szer, M.B., B.S., Nicholas Jackson, M.B., B.S., M.D., Peter G. Bardy, M.B., B.S.,
Dianne Plews, M.B., Ch.B., Simon Lyons, M.B., Ch.B., Linley Bielby, B.N., M.H.A.,
Erica M. Wood, M.B., B.S., and Michael F. Murphy, M.B., B.S., M.D., for the TOPPS Investigators®
TOPPS: Time to ≥ grade 2 bleeding episode
Therapeutic Platelet Transfusion

• Little evidence to guide practice
• Targeted PLT count depends on severity of bleeding
  • Petechiae/bruising: PLT >10 x 10^9/L
  • Mucosal: PLT >20 x 10^9/L
  • Major hemorrhage: PLT >50 x 10^9/L
  • Intracranial/ophthalmologic: PLT >80-100 x 10^9/L
• Platelet dysfunction regardless of count
Are platelet transfusions the answer for all situations with severe thrombocytopenia...?
Platelet transfusion may be ineffective or even harmful...

• Ineffective:
  • HLA sensitization
  • ITP*
  • In presence of certain drugs
  • Splenic sequestration
  • Antiplatelet agents

• Harmful:
  • Thrombotic thrombocytopenic purpura (TTP)
  • Heparin-induced thrombocytopenia
  • Anti-platelet agents and intracranial hemorrhage
Platelet transfusion associated with thrombosis in TTP and HIT

Goel et al. Blood 2015
Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial

PATCH Trial results
Case A

• 44-year-old mother of three children
• Admitted with leukemia in stable clinical status
• Treatment-related thrombocytopenia with PLT $8 \times 10^9$/L
• Transfused 3 units of WBD platelets without improvement in PLT
• Transfusion history: 3 non-leukoreduced transfusions, 1 complicated by febrile reaction
Platelet recovery and survival

• Goal of most platelet transfusions is to increase platelet count

• Several factors affect platelet recovery and survival following transfusion:
  • Unit-dependent factors
  • Patient-dependent factors
Platelet Refractoriness

- Poor platelet count increment following blood transfusion
- PLT count should be measured 30-60 minutes after transfusion
- Corrected count increment (CCI) <5.5-7.5

\[
CCI = \frac{(PLT \text{ increment } \times BSA)}{PLT \text{ dose}}
\]
Factors affecting platelet recovery and survival

• Unit-dependent
  • Number of platelets in unit
  • Time from collection
  • pH during storage
  • Temperature during storage*

Murphy et al. NEJM. 1969
Factors affecting platelet recovery and survival

Non-immune
- Patient blood volume
- Drugs
  - Vancomycin
  - Cephalosporins
  - Amphotericin B
- Splenomegaly
- Fever
- Sepsis
- Graft-vs-host disease
- Vasculitis

Immune
- HLA antibodies
- HPA antibodies
- ABO antibodies
- ITP
Case A

- No clinical bleeding
- Afebrile
- Not on any antibiotics
- No splenomegaly on imaging 6 months earlier, no clinical evidence of splenomegaly
- PLT count done 1 hour after PLT transfusion showed increment of 2

- HLA antibody screen positive with cPRA of 94%!
Q1: What is the main difference between apheresis and whole-blood derived platelets?
   a. Apheresis platelets are more effective
   b. The collection methods
   c. Whole-blood derived platelets are more effective
   d. Fewer donor exposures with whole-blood derived platelets
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Q2: Which of the following is not a reason for platelet refractoriness?
   a. HLA antibodies
   b. Splenomegaly
   c. Sepsis
   d. Co-infusion with saline
Which of the following is not a reason for platelet refractoriness?

- HLA antibodies
- Splenomegaly
- Sepsis
- Co-infusion with saline
Q3: Which of the following patients is unlikely to benefit from platelet transfusion?
   a. 60M with sub-arachnoid hemorrhage on ASA, PLT 140 x 10⁹/L
   b. 45M with AML, not bleeding, PLT 8 x 10⁹/L
   c. 29F pregnant, going for C-section for HELLP, PLT 20 x 10⁹/L
   d. 65F bleeding post-CABG, PLT 35 x 10⁹/L
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Any Questions for Dr. Mack?
Thank You