

Platelet Transfusion: Back to Basics

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The Ottawa Hospital

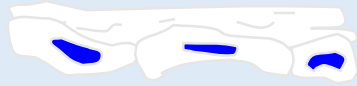
University of Ottawa

Outline

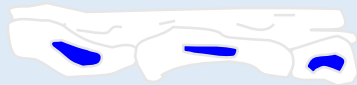
- Role platelets play in hemostasis
- Modes of production of platelet concentrates
- Indications for platelet transfusion
- Situations in which platelet transfusion may be ineffective or harmful
- Factors associated with poor recovery and survival of platelets

Clot formation

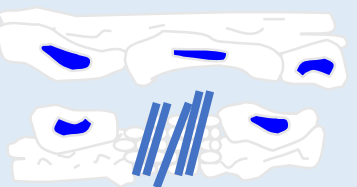
Vessel Wall Injury



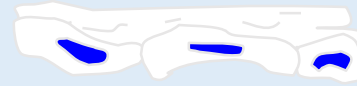
Platelet Adhesion



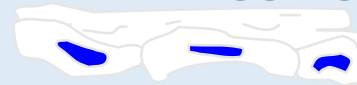
Fibrin Formation



Vessel Wall Contraction

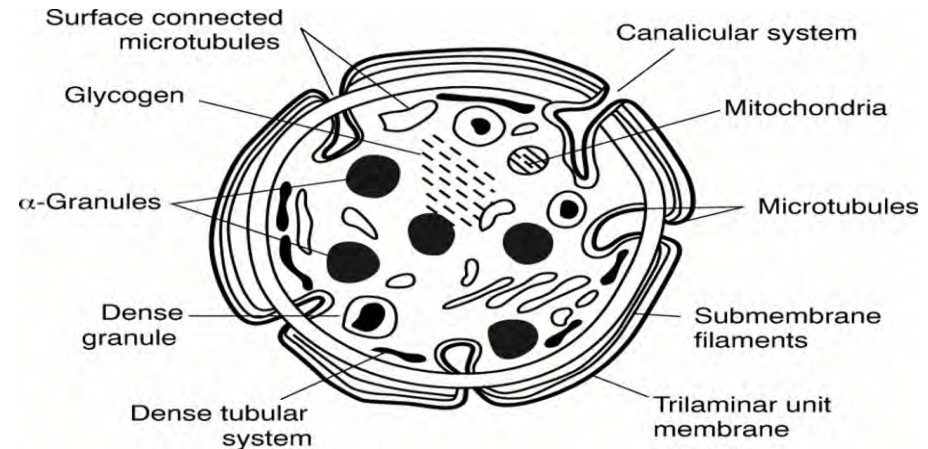


Platelet Aggregation



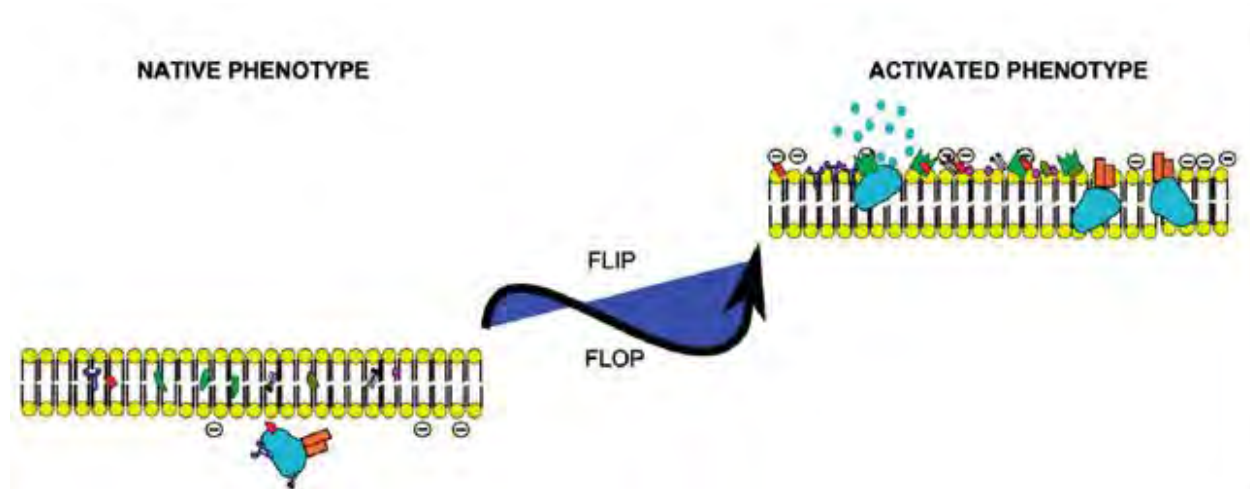
Primary clot formation: the platelet plug

- 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

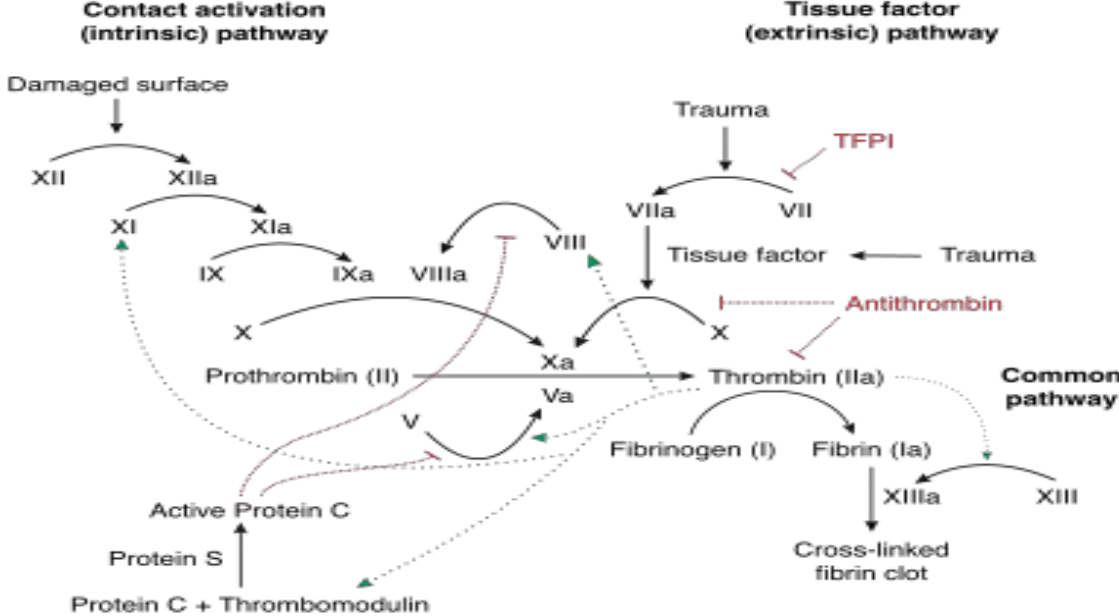


Thrombin and Fibrin formation

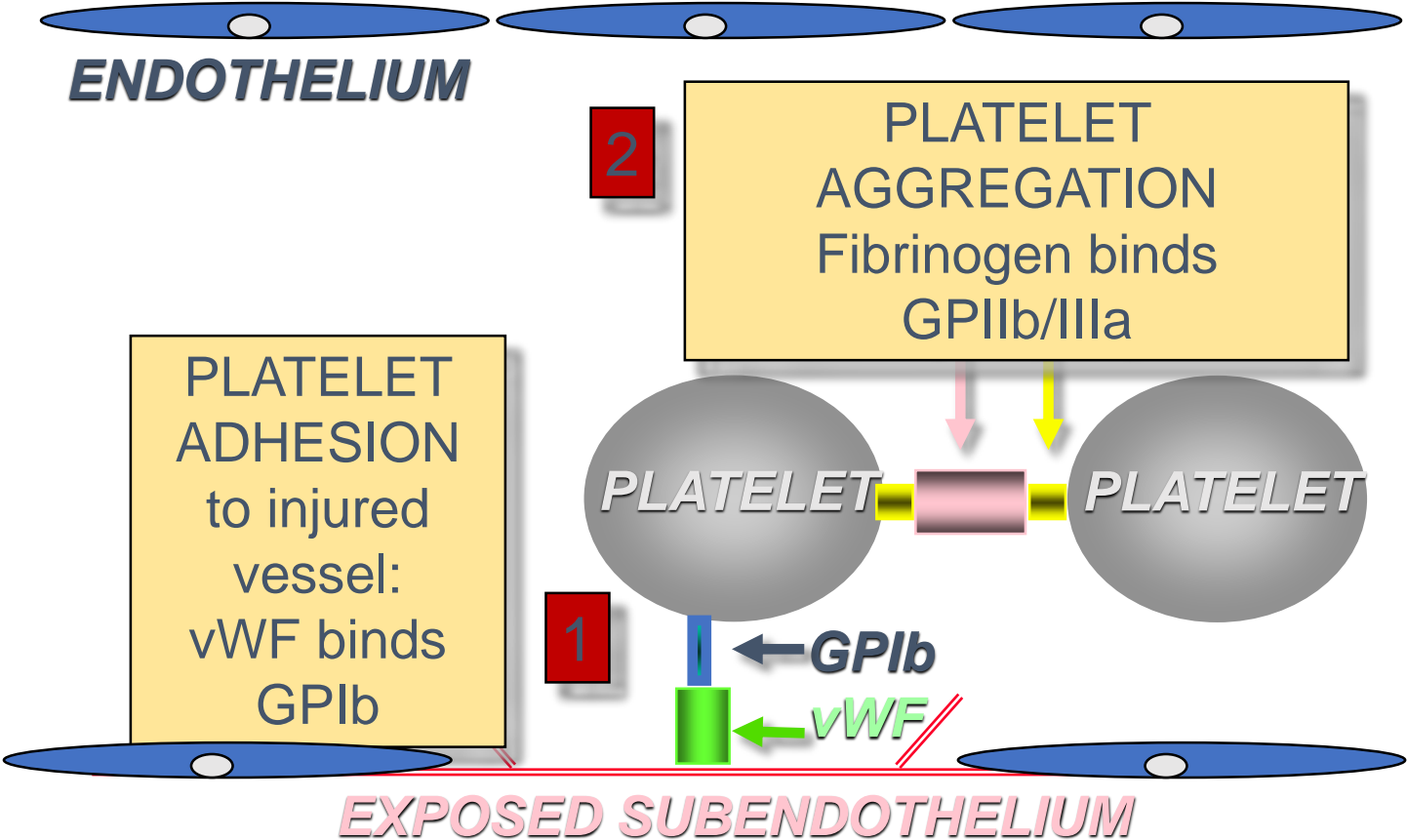
- Negative platelet surface provides platform for clotting 'cascade' resulting ultimately in thrombin generation, conversion of fibrinogen to fibrin, and secondary clot formation



The clotting cascade



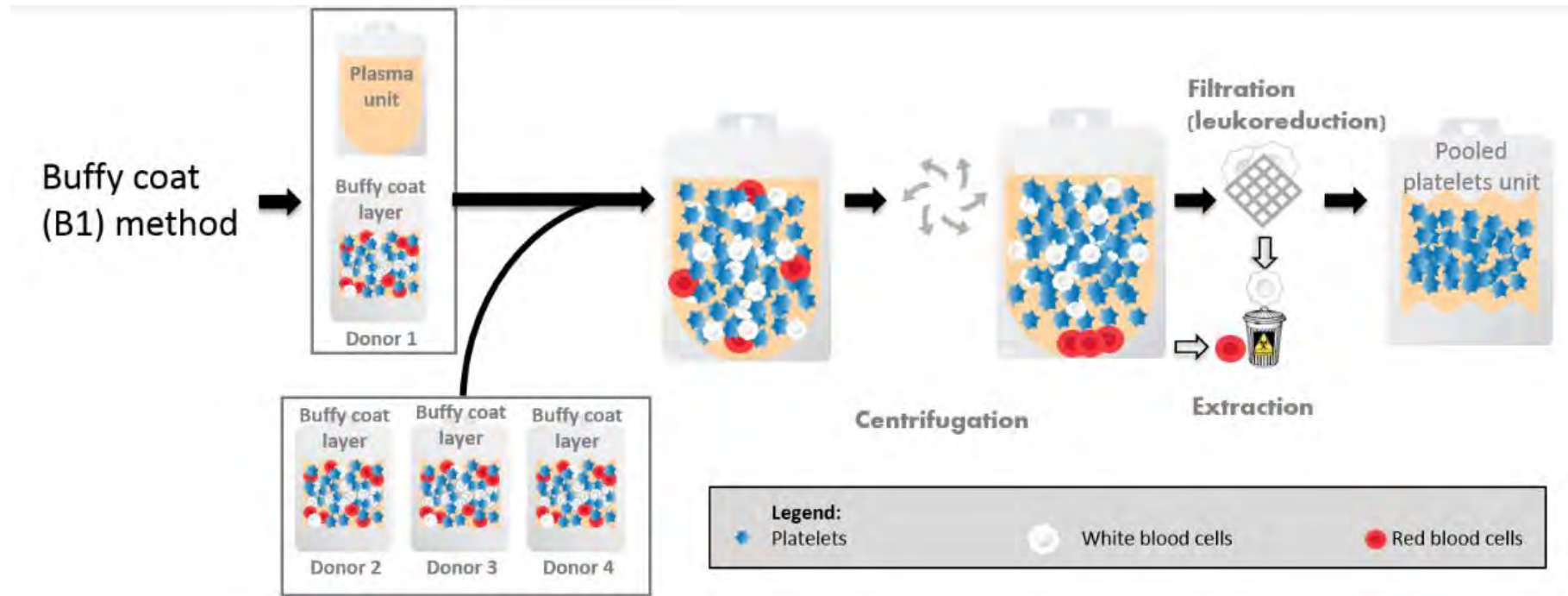
Platelet Plug Formation



Modes of Production



Whole Blood Derived (WBD)



Apheresis platelet concentrates



Platelet units

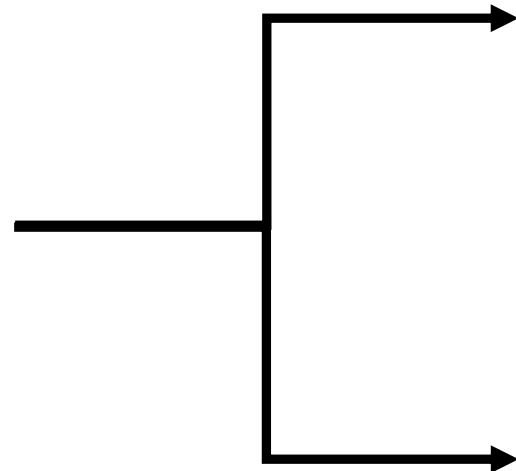
Pooled Platelets (WBD)

- Volume 330-360 mL
- $\sim 300 \times 10^9$ 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
- $\sim 370 \times 10^9$ 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 $PLT < 100 \times 10^9/L$



TOPPS Trial

The **NEW ENGLAND**
JOURNAL *of* **MEDICINE**

ESTABLISHED IN 1812

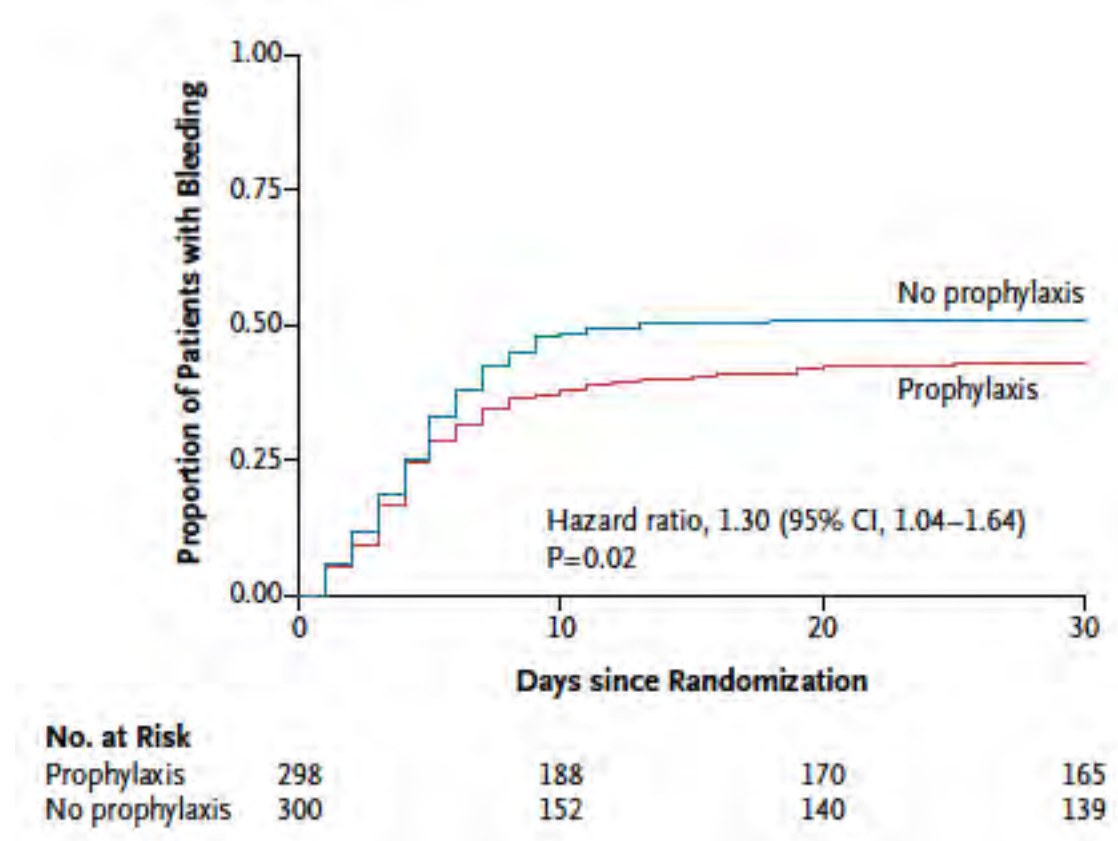
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A No-Prophylaxis Platelet-Transfusion Strategy for Hematologic Cancers

Simon J. Stanworth, M.D., D.Phil., Lise J. Estcourt, M.B., B.Chir., Gillian Powter, B.A.,
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 \geq grade 2 bleeding episode



Therapeutic Platelet Transfusion

- Little evidence to guide practice
- Targeted PLT count depends on severity of bleeding
- Petechiae/bruising: PLT $>10 \times 10^9/L$
- Mucosal: PLT $>20 \times 10^9/L$
- Major hemorrhage: PLT $>50 \times 10^9/L$
- Intracranial/ophthalmologic: PLT $>80-100 \times 10^9/L$
- Platelet dysfunction regardless of count



Are platelet transfusions the answer for all situations with severe thrombocytopenia...?



Platelet transfusion may be ineffective or even harmful...

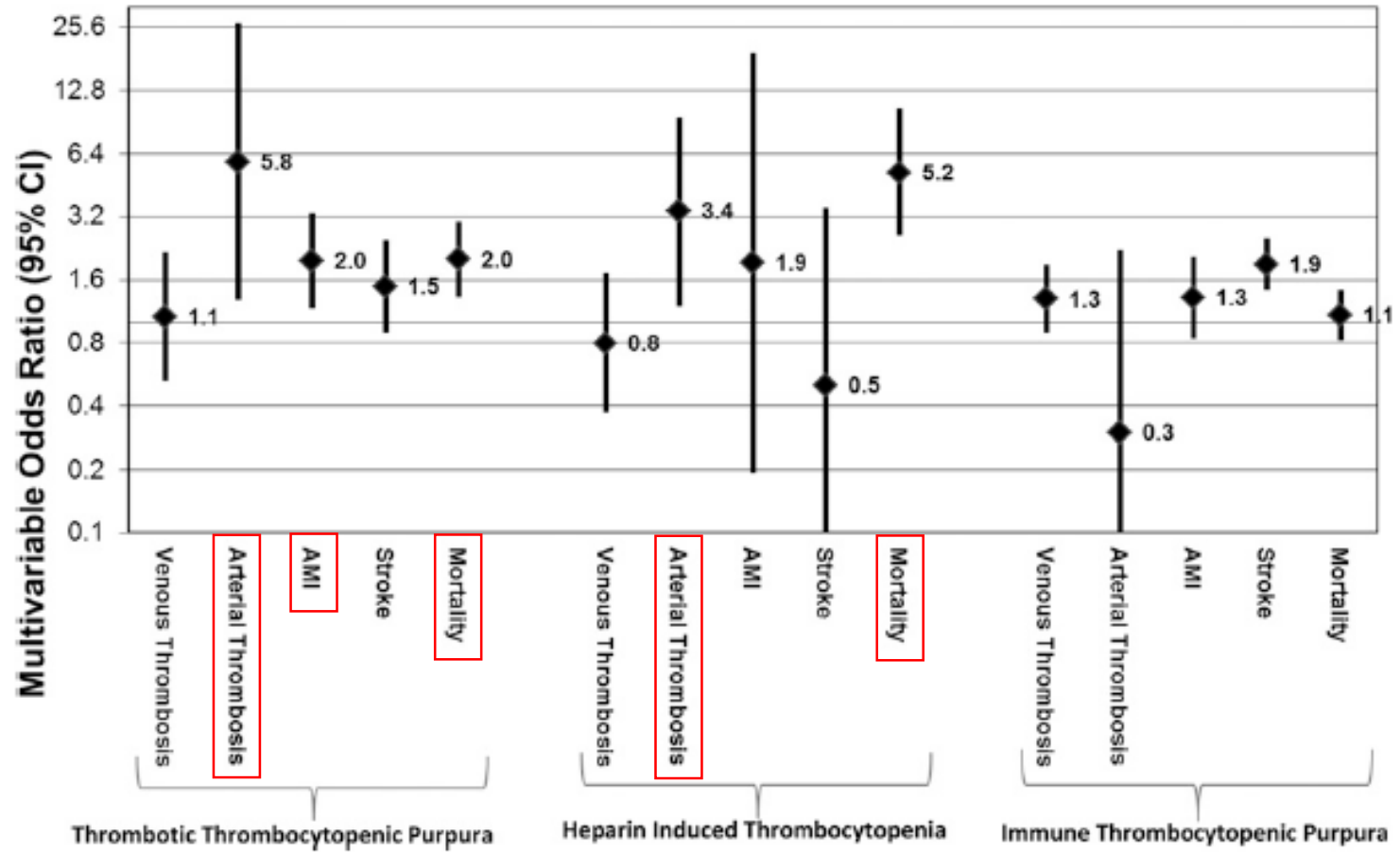
- Ineffective:

- 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



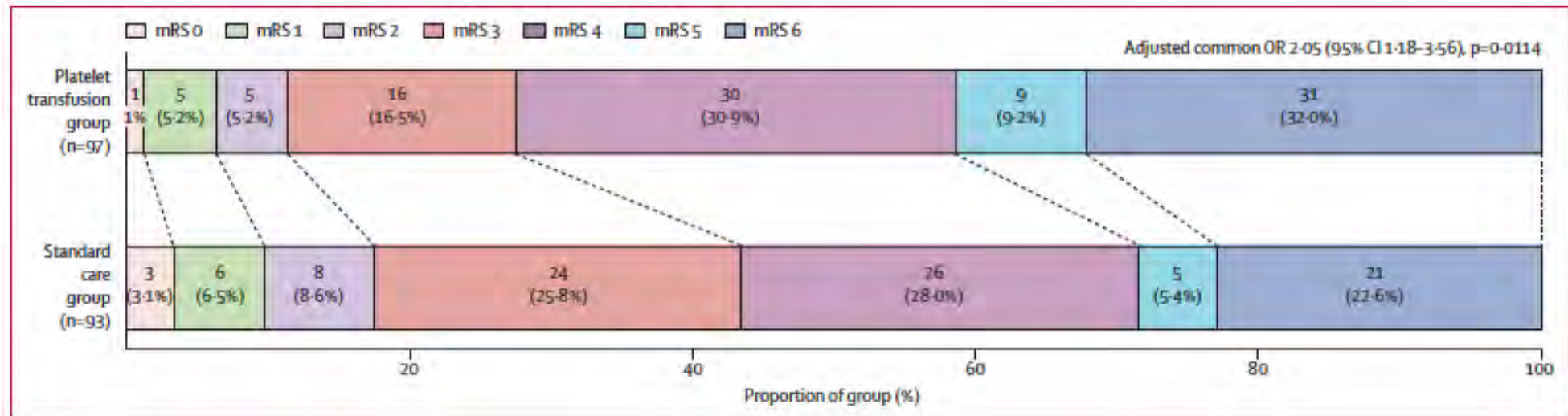
PATCH Trial

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

M Irem Baharoglu, Charlotte Cordonnier*, Rustam Al-Shahi Salman*, Koen de Gans, Maria M Koopman, Anneke Brand, Charles B Majoie, Ludo F Beenen, Henk A Marquering, Marinus Vermeulen, Paul J Nederkoorn, Rob J de Haan, Yvo B Roos, for the PATCH Investigators†*

PATCH Trial results

	Platelet transfusion group (n=97)	Standard care group (n=93)	Odds ratio (95%CI)	p value
Alive at 3 months (survival)	66 (68%)	72 (77%)	0.62 (0.33-1.19)	0.15
mRS score 4-6 at 3 months	70 (72%)	52 (56%)	2.04 (1.12-3.74)	0.0195
mRS score 3-6 at 3 months	86 (89%)	76 (82%)	1.75 (0.77-3.97)	0.18
Median ICH growth at 24 h (mL)*	2.01 (0.32-9.34)	1.16 (0.03-4.42)	..	0.81



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

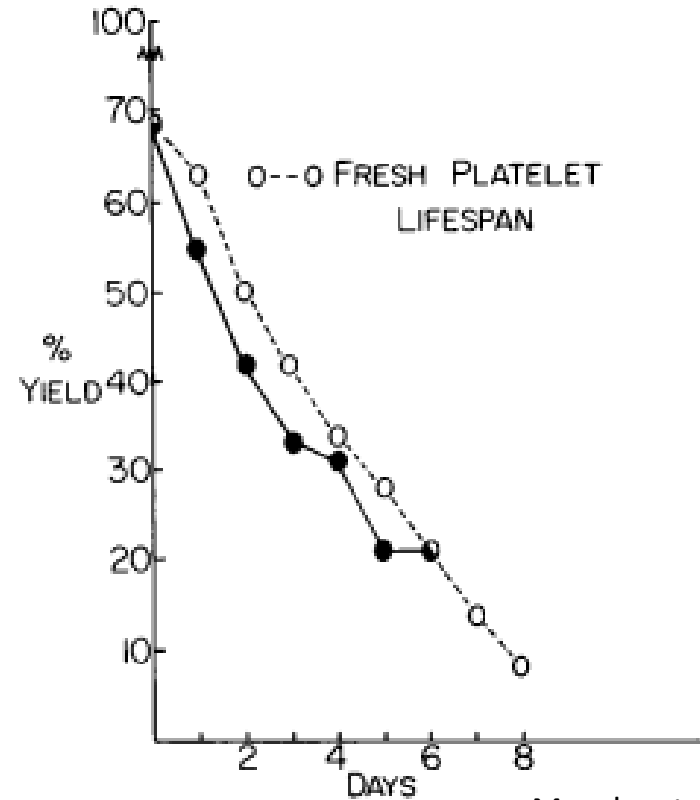
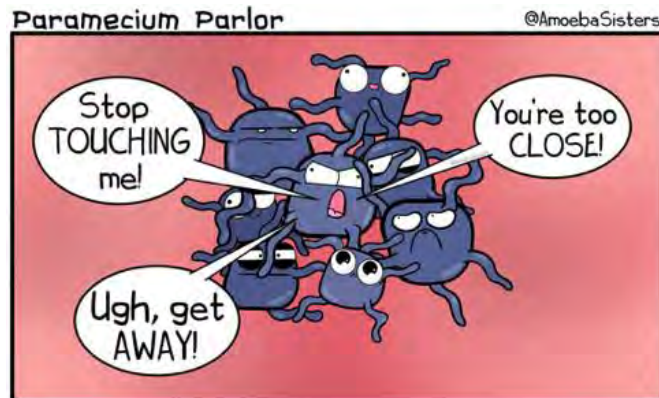
- Poor platelet count increment following blood transfusion
- PLT count should be measured 30-60 minutes after transfusion

- Corrected count increment (CCI) <5.5-7.5

$$CCI = (PLT \text{ increment} \times BSA) \div PLT \text{ dose}$$

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%!

Questions for Case A

Top

JEOPARDY!

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

What is the main difference between apheresis and whole-blood derived platelets?

Apheresis platelets are more effective

The collection methods

Whole-blood derived platelets are more effective

Fewer donor exposures with whole-blood derived platelets

JEOPARDY!

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

JEOPARDY!

Q3: Which of the following patients is unlikely to benefit from platelet transfusion?

- a. 60M with sub-arachnoid hemorrhage on ASA, PLT $140 \times 10^9/L$
- b. 45M with AML, not bleeding, PLT $8 \times 10^9/L$
- c. 29F pregnant, going for C-section for HELLP, PLT $20 \times 10^9/L$
- d. 65F bleeding post-CABG, PLT $35 \times 10^9/L$

Which of the following patients is unlikely to benefit from platelet transfusion?

60M with sub-arachnoid hemorrhage
on ASA, PLT 140 x 10⁹/L

45M with AML, not bleeding, PLT 8 x
10⁹/L

29F pregnant, going for C-section for
HELLP, PLT 20 x 10⁹/L

65F bleeding post-CABG, PLT 35 x
10⁹/L

Any Questions for Dr. Mack?

Top



Thank You