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April 10, 2019

Patient Case Studies: Sticky Situations For Platelet Transfusions

Disclosures

- Ad Board: Celgene, Jansen, Takeda, Roche, Sanofi, Leo, Shire, Servier, Phizer, Teva, Lundbeck
- Honoraria: Teva, Jansen, Sanofi, Leo, Lundbeck

Dr. Jeannie Callum

"About once a year our hospital requires special blood to be brought in from far away for a patient in need and never has the donor refused. Never. The altruistic spirit of blood donors never ceases to amaze me."

Dr. Jeannie Callum
Sunnybrook Health Sciences Centre

Objectives

- General risks and benefits of platelet transfusions
- Importance of platelet transfusion in the prevention and treatment of bleeding in patients with treatment or disease related thrombocytopenia.
- Avoid overuse of platelet transfusions
- Indications for platelet transfusion for patients with cancer
- Indications for platelet transfusion in patients undergoing hematopoietic stem cell transplant
- Indications for platelet transfusion in patients with hematologic malignancies or solid tumours who require invasive procedures

AML Patient case:

- 25 year old male presents to the Emergency department with a one week history of fever and gingival bleeding.
- Labs: WBC 2.2 X 10 9/L, hemoglobin of 68 g/L and platelets of 8 X 10 9/L. PT and PTT and fibrinogen are normal.
- A bone marrow biopsy reveals a new diagnosis of Acute Myeloid Leukemia. In order to start 3 + 7 induction chemotherapy a central line will be needed.

The Interventional Radiologist wants platelets transfused to reduce the risk of bleeding with the insertion of a central line.

How many pools of platelets are necessary prior to the procedure?

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- Should he receive prophylactic platelet transfusions?
- At what platelet count should platelets be transfused?

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- Should he receive prophylactic platelet transfusions?
- At what platelet count should platelets be transfused?
- What about if he has a fever? Does this impact the threshold for platelet transfusion?

Autologous stem cell transplant patient case

A 62 year old male Day 8 post autologous stem cell transplant for multiple myeloma has a platelet count of 9 X 10 9/L and is admitted to the Complex Malignant Hematology ward.

He is feeling well and has no evidence of bleeding.

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- Does he need a prophylactic platelet transfusion?

Platelet transfusions in patients with cancer: Which patients benefit?

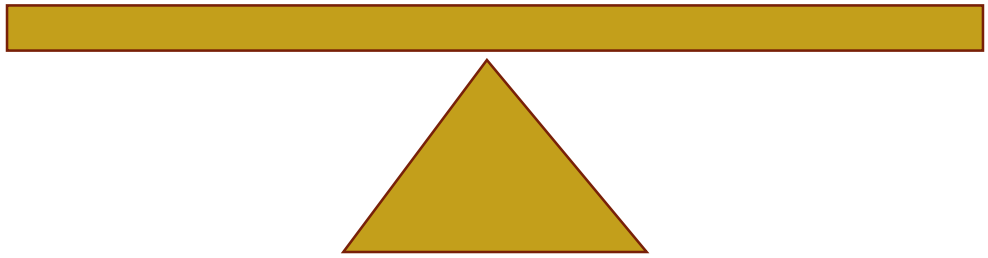
Prevention of bleeding

Treatment of active bleeding

Cost of platelet transfusions

Potential adverse effects:

- **Fever**
- **Allergic reactions**
- **Transfusion related lung injury**
- **Bacterial contamination**



Risks of Platelet Transfusions

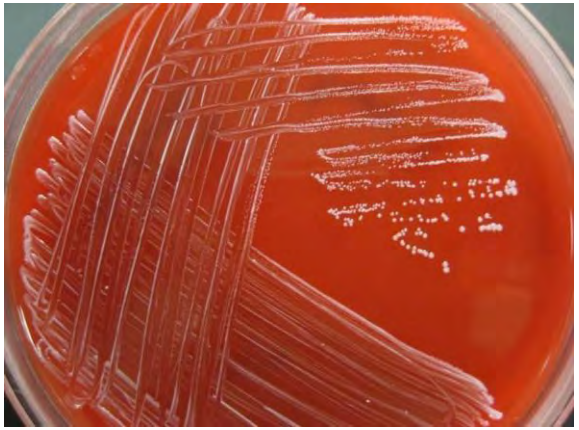
- Febrile non-hemolytic transfusion reaction (1 in 20)
- Urticarial reaction (1 in 100)
- Bacterial sepsis (1 in 10,000)
- Acute hemolytic reaction: group O platelet to a non-O recipient "Dangerous Group O Donor"

Risks of hemolysis due to anti-A and anti-B caused by the transfusion of blood or blood components containing ABO-incompatible plasma

Probiotic-associated high-titer anti-B in a group A platelet donor as a cause of severe hemolytic transfusion reactions

Bacterial Sepsis from Platelets

- Blood agar plate vs. hematologist
- Agar 20, hematologists *zero*
- 1 in 2,600 infected (n=20)
- 1 in 10,000 symptomatic sepsis (n=5)
  - All hematology patients
  - 4 of 5 were outpatients
  - Onset 9-24 hours post-transfusion
  - All moderate to life-threatening
  - 1 death
  - None recognized as bacterial contamination



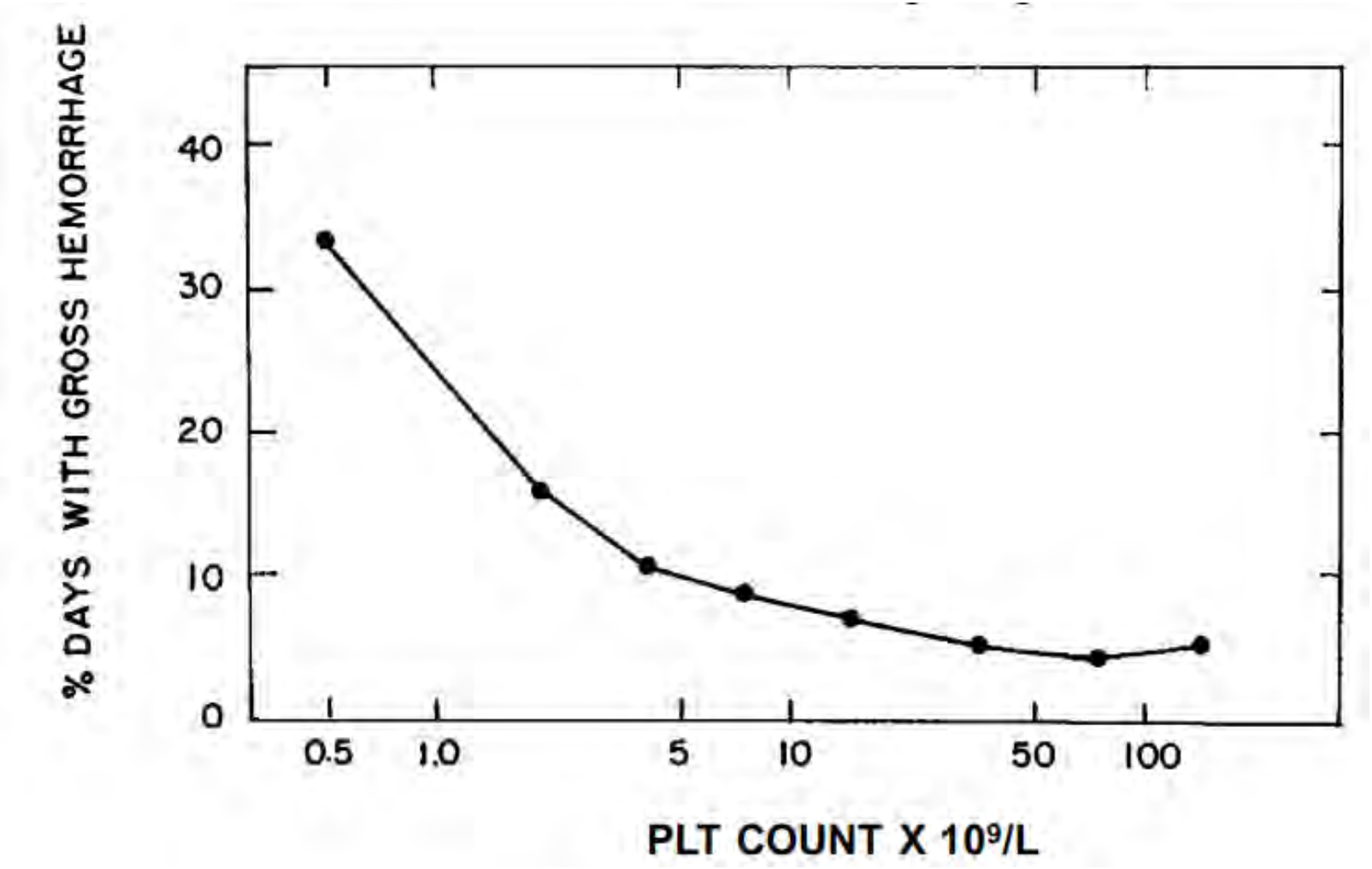
BLOOD, 28 JANUARY 2016 • VOLUME 127, NUMBER 4

When to transfuse platelets?

There is evidence to make decisions for platelet transfusions in the setting of cancer associated thrombocytopenia

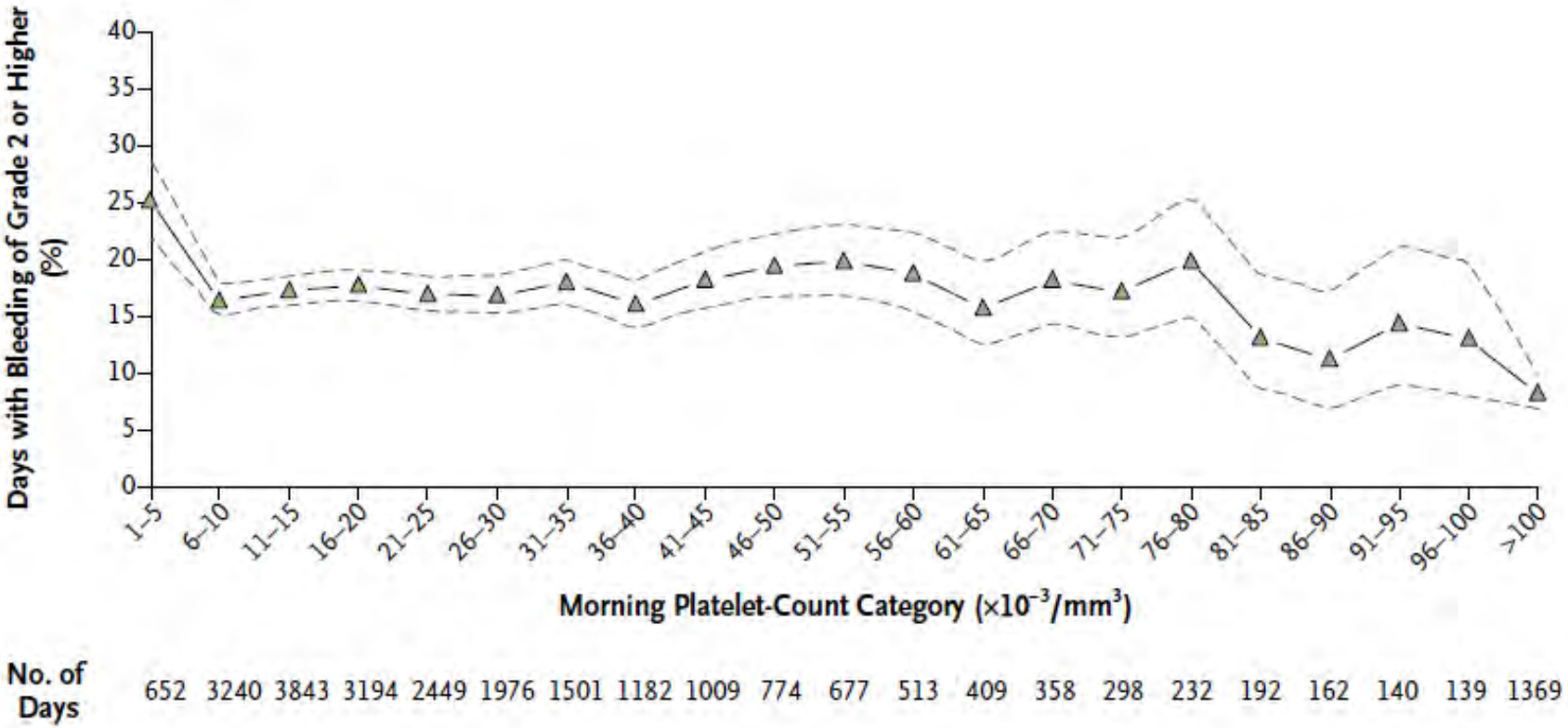

Multiple randomized trials
and large cohort studies
to
Inform decisions

Do PLT transfusions prevent bleeding in patients with thrombocytopenia?



Gaydos et al. NEJM 1962; 266: 9

PLADO



No escalation to <20 for febrile/septic/sick patients

Slichter S et al. NEJM 2010; 362: 600

Wandt Study (n= 396; AML or autoHSCT)

Bleeding	PLT prophylaxis	No prophylaxis	P value
Grade 2+ (minor)	65 (19%)	127 (42%)	<0.0001
Grade 3 (need Tx)	3 (1%)	7 (2%)	0.21
Grade 4 (CNS or Fatal)	4 (1%)	14 (5%)	0.02

No escalation to <20 for febrile/septic/sick patients

Wandt et al. Lancet 2012; 380: 1309

Wandt subgroup analysis

	PLT prophylaxis	No prophylaxis	P value
Grade 2+	57 (24%)	98 (51%)	<0.0001
Grade 3	3 (1%)	6 (3%)	0.32
Grade 4	4 (2%)	13 (7%) **2 Fatal**	0.01

- AutoHSCT (n=201)

	PLT prophylaxis	No prophylaxis	P value
Grade 2+	8 (8%)	29 (28%)	0.0005
Grade 3	0 (0%)	1 (1%)	1.0
Grade 4	0 (0%)	0 (0%)	-

Wandt et al. Lancet 2012; 380: 1309

Stanworth Study (n= 600; Chemo for hematologic malignancy or autoHSCT)

Bleeding	PLT prophylaxis	No prophylaxis	P value
Grade 2+ (minor)	128 (43%)	151 (50%)	0.06
Grade 3 (need Tx)	3 (1%)	7 (2%)	NS
Grade 4 (CNS or Fatal)	0 (0%)	2 (1%)	NS

For autoHSCT patients – no difference in bleeding rates (2-4)

No escalation to <20 for febrile/septic/sick patients

Stanworth S, et al. NEJM 2013; 369: 1771

What is the appropriate threshold for prophylactic platelet transfusion in the setting of HSCT?

- The ASCO guidelines continue to recommend prophylactic transfusion of platelets if < 10 X 10 9/L in adult patients undergoing **allogeneic stem cell transplant**.

- For Adult patients undergoing **autologous stem cell transplant**, randomized trials show similar rates of bleeding and decreased platelet transfusion when patients are transfused at first sign of bleeding rather than prophylactically. This is the practice in experienced centers.

Close observation is required if using a therapeutic transfusion approach.

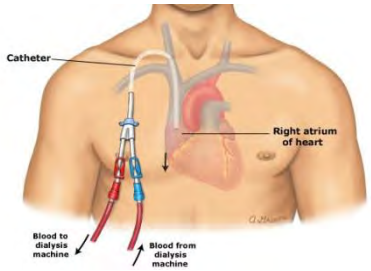
TYPE OF RECOMMENDATION: Evidence based; Evidence quality HIGH. Strength of recommendation: moderate

What about platelet threshold for procedures in the setting of thrombocytopenia?

Central line insertions?
Thoracentesis?
Paracentesis?
Liver biopsy?

What do the trials tell us about platelet thresholds for procedures?

Minor procedure: CVL



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PLT	n	Bleeds (>compression)
<25	42	0
20-49	302	0

- Zeidler et al (n=604 non-tunneled in AML pts)

PLT	n	Bleeds*	OR
<20	14	8 (57%)	2.84 (1.34-6.02)
20-49	156	50 (32%)	1.45
50-99	140	49 (35%)	1.48
>99	272	74 (27%)	1.00

***96% grade 1 (bruise); 4% grade 2 (pressure)**

Haas et al. J Vasc Int Rad 2010; 21:2
Zeidler et al. Transfusion 2011; 51: 2269

Minor procedure: LP

PLT	N	Bleeds
≤20	199	0
21-50	742	0

- 195 LPs in adults

PLT	N	Bleeds	>500 RBC
21-30	35	0	6
31-50	40	0	4
51-100	43	0	3
>101	77	0	1

Howard et al. JAMA 2000; 284: 2222
Vavricka et al. Ann Hematol 2003; 82: 570

Minor procedures: Liver Biopsy

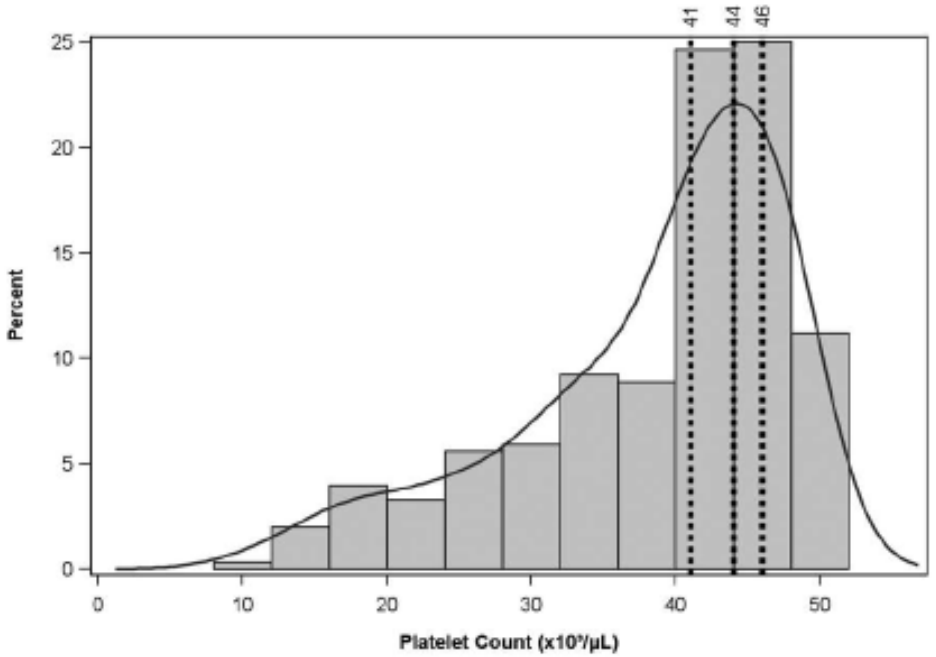
PLT	No Bleeding	Bleeding	p
≤50	90 (97.8%)	2 (2.2%)	0.04
>50	6449 (99.5%)	31 (0.5%)	

- AASLD: management of patients scheduled for liver biopsy:
  - The decision to perform liver biopsy in the setting of abnormal laboratory parameters of hemostasis should continue to be reached as the result of local practice(s) and consideration of the risks and benefits of liver biopsy ***because there is no specific PT-INR and/or platelet count cutoff at or above which potentially adverse bleeding can be reliably predicted*** (Class I, Level C).
  - Platelets should be considered when levels are **<50-60 x 10^9/L** (both transcutaneously or transvenously) (Class I, Level C).

Boyum Mayo Clin Proc 2016; 91: 329
Rockey DC, et al. Hepatology. 2009;49(3):1017-44

Minor procedures: paracentesis

- 304 paracenteses in patients with PLT<50
- 3 bleeds (41, 44, 46)
- 2 patients on dialysis
- All controlled with post-procedure transfusion (no fatal bleeding)
- Conclusion: Don't check the platelet count and don't intervene pre-procedure



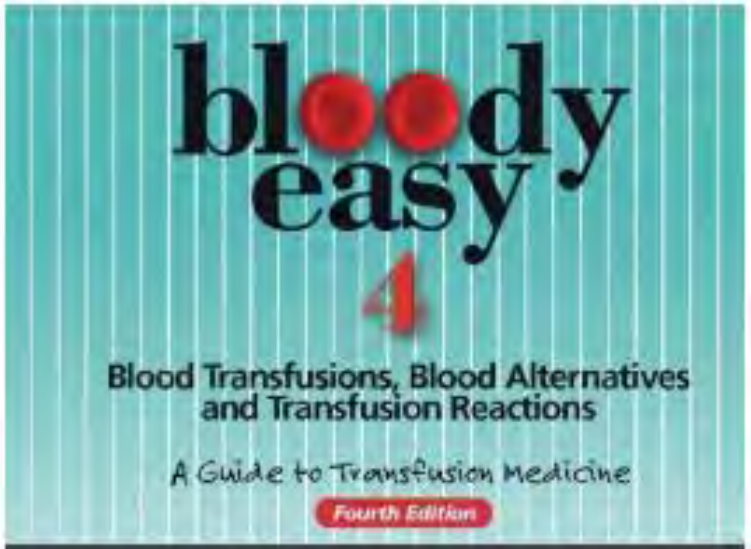
Kurup et al. J Ultrasound Med 2015; 34: 1833-1838

Minor Procedure: thoracentesis

- 436 patients undergoing thoracentesis

	Blind	US Guided	P-value
No bleed (n=38)	6 (67%)	32 (100%)	
Bleed (n=3)	3 (33%)	0 (0%)	
All (n=41)	9 (100%)	32 (100%)	0.03

Orlandi et al. Clin Respir J 2018; 12:1747



Latest Edition Now Available!
Bloody Easy 4: Blood Transfusions, Blood Alternatives and Transfusion Reactions. A Guide to Transfusion Medicine Fourth Edition
inventory.transfusionontario.org

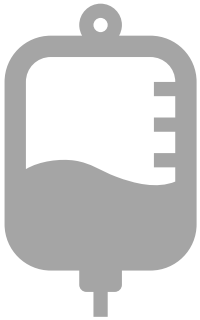
PLT (x 10⁹/L)	Clinical Setting	Suggest
<10	Non-immune thrombocytopenia	Transfuse 1 pool of platelets[45]
<10	Non-immune thrombocytopenia & HLA-alloimmunized	Transfuse 1 unit of HLA-matched apheresis platelets[45]
<20	Procedures not associated with significant blood loss (e.g., central line placement)	Transfuse 1 pool of platelets[15]
20-50	Procedures not associated with significant blood loss	1 pool of platelets on hold, transfuse only if significant bleeding[38]
<30	Patient on anticoagulants that should not be stopped	Transfuse 1 pool of platelets
<50	Epidural anesthesia and lumbar puncture	Transfuse 1 pool immediately before procedure[15,47]
<50	Procedures associated with blood loss or major surgery (>500 mL expected blood loss)	Transfuse 1 pool immediately before procedure[38,48]
<50	Immune thrombocytopenia	Transfuse platelets only with life-threatening bleeding[49]
<100	Pre-neurosurgery or head trauma	Transfuse 1 pool of platelets[50,51]
Any	Platelet dysfunction and marked bleeding (e.g., post cardiopulmonary bypass). Exception: Transfusing platelets for intracranial hemorrhage not requiring surgical management in patients on antiplatelet agents leads to increased morbidity	Transfuse 1 pool of platelets[38,52]

Bloody Easy 4, 2017

ATTENTION

The transfusion of platelets to non-operative patients with ICH on ASA/clopidogrel increases the risk of disability at 3 months.

CRITICAL TO ASSESS THE PLATELET COUNT 10 MINUTES POST INFUSION PRIOR TO INVASIVE PROCEDURES.



DO NOT ASSUME ADEQUATE PLATELETS SIMPLY BECAUSE THEY HAVE RECEIVED A PLATELET TRANSFUSION.

What about prophylactic platelet transfusion in patients with chronic, stable, severe thrombocytopenia, who are not on treatment?

- Patients with myelodysplasia or aplastic anemia not receiving treatment may be observed without prophylactic platelet transfusions.
- Platelets are transfused for active bleeding or if patient is receiving active treatment.

No randomized studies. Many such patients may not experience severe bleeding over long periods of time in spite of significant thrombocytopenia

TYPE OF RECOMMENDATION: informal consensus; Evidence quality: intermediate; Strength of recommendation: moderate.

JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

Platelet Transfusion for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update

Charles A. Schiffer, Kari Bohlke, Meghan Delaney, Heather Hume, Anthony J. Magdalinski, Jeffrey J. McCullough, James L. Omel, John M. Rainey, Paolo Rebulla, Scott D. Rowley, Michael B. Troner, and Kenneth C. Anderson

Contents lists available at ScienceDirect

Transfusion Medicine Reviews

journal homepage: www.tmreviews.com

Guidelines

Guidance on Platelet Transfusion for Patients With Hypoproliferative Thrombocytopenia

Annals of Internal Medicine | CLINICAL GUIDELINE

Platelet Transfusion: A Clinical Practice Guideline From the AABB

Richard M. Kaufman, MD; Benjamin Djulbegovic, MD, PhD; Terry Gernsheimer, MD; Steven Kleinman, MD; Alan T. Tinmouth, MD; Kelley E. Capocelli, MD; Mark D. Cipolle, MD, PhD; Claudia S. Cohn, MD, PhD; Mark K. Fung, MD, PhD; Brenda J. Grossman, MD, MPH; Paul D. Mintz, MD; Barbara A. O'Malley, MD; Deborah A. Sesok-Pizzini, MD; Aryeh Shander, MD; Gary E. Stack, MD, PhD; Kathryn E. Webert, MD, MSc; Robert Weinstein, MD; Babu G. Welch, MD; Glenn J. Whitman, MD; Edward C. Wong, MD; and Aaron A.R. Tobian, MD, PhD

What about prophylactic platelet transfusion in patients with solid tumours?

- The risk of bleeding during chemotherapy-induced thrombocytopenia **depends on the severity of the thrombocytopenia and the duration of the platelet nadir**.
- A threshold of <10 X 10 9/L for prophylactic platelet transfusion is extrapolated from studies in Hematologic malignancies.
- A higher threshold is appropriate in patients with active localized bleeding seen in some necrotic tumour types: gynecologic, colorectal, melanoma or bladder tumours. Transfusion at a higher threshold of 20 X 10 9/L could be considered.

Type of recommendation: informal consensus; Evidence quality: low; Strength of recommendation: moderate.

Summary

- When should you give 1 pool of platelets?
- Use the clinical trial data where available and guidelines as guardrails.
- Utilize platelet resources wisely.

035: Why Give Platelets? with Rick Kaufman

Platelets are tiny, but they can be a big issue! Dr. Rick Kaufman magnifies what the evidence shows about platelet transfusion.

Listen to This Episode!

Blood Bank Guy

016: Plasma Transfusion with Jeannie Callum

As many as 50% of plasma transfusions are unnecessary or inappropriate! You need to know why, and Dr. Jeannie Callum explains it SO well!