Manejo de la transfusión de plaquetas

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Thrombocytopenia

- Common in ICU setting
  - 25-38% with< 100,000/μL
  - 2-3 % with < 10,000/μL
- Common etiologies
  - Drug-induced: heparin, antibiotics, H2 blockers
  - Infection
  - Underlying clinical conditions
- Less frequent causes: ITP, TTP

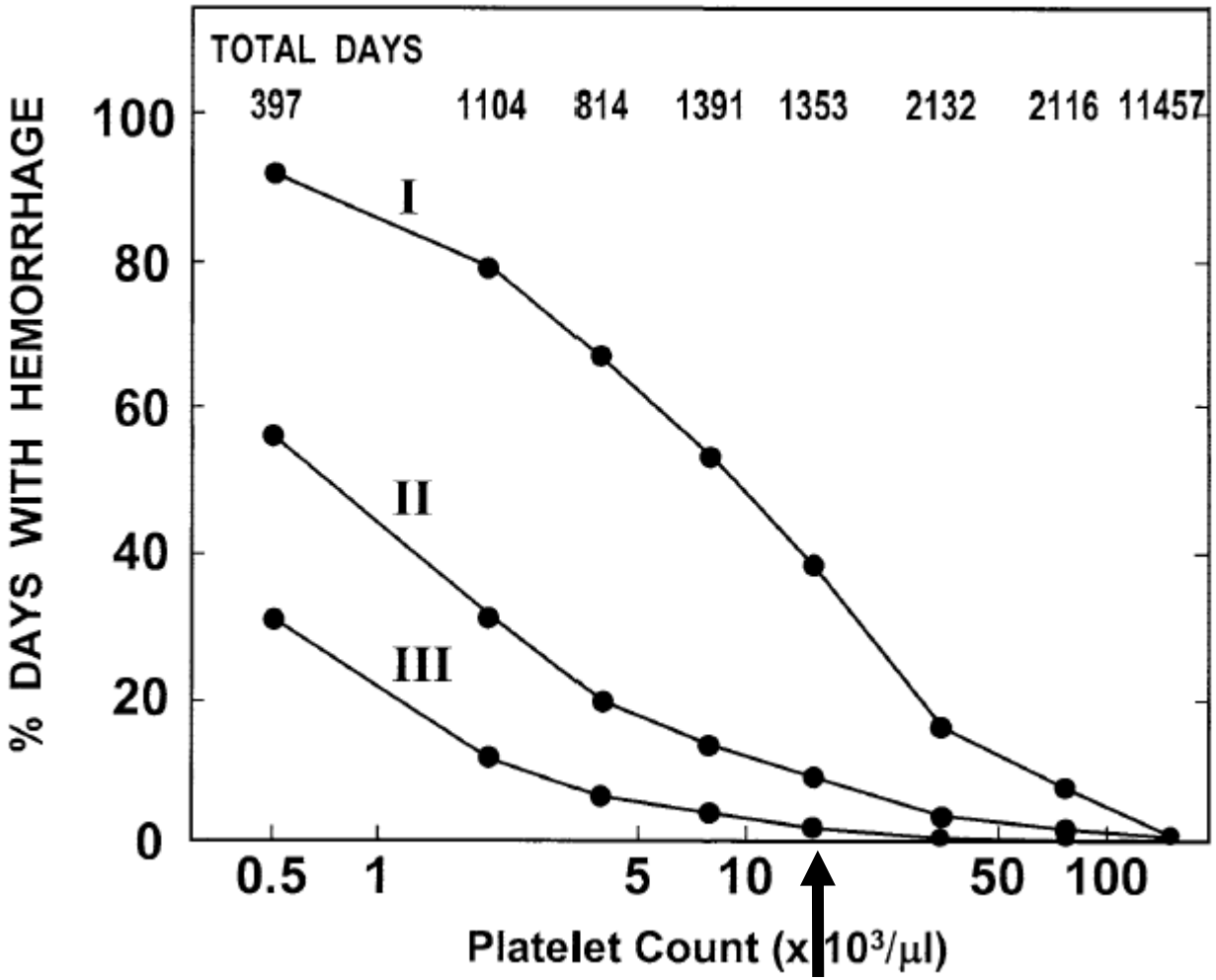
Platelet dysfunction

- Antiplatelet agents
  - All!
- Renal disease
  - Uremia
- Liver disease
- Myeloproliferative disorders
- Congenital
  - Prophylaxis is important!

Bleeding risk assessment

- Screening lab tests
  - PT and aPTT: become abnormal before hemostatic levels have been compromised
  - Thrombocytopenia: evaluate peripheral smear to r/o pseudo thrombocytopenia, size and appearance of plts
  - Platelet function assays: limited by platelet count
- If abnormal: allow time for further evaluation

How low can platelet counts get before patients bleed spontaneously? Gavdos et al. (1962) NEJM 266:905-909



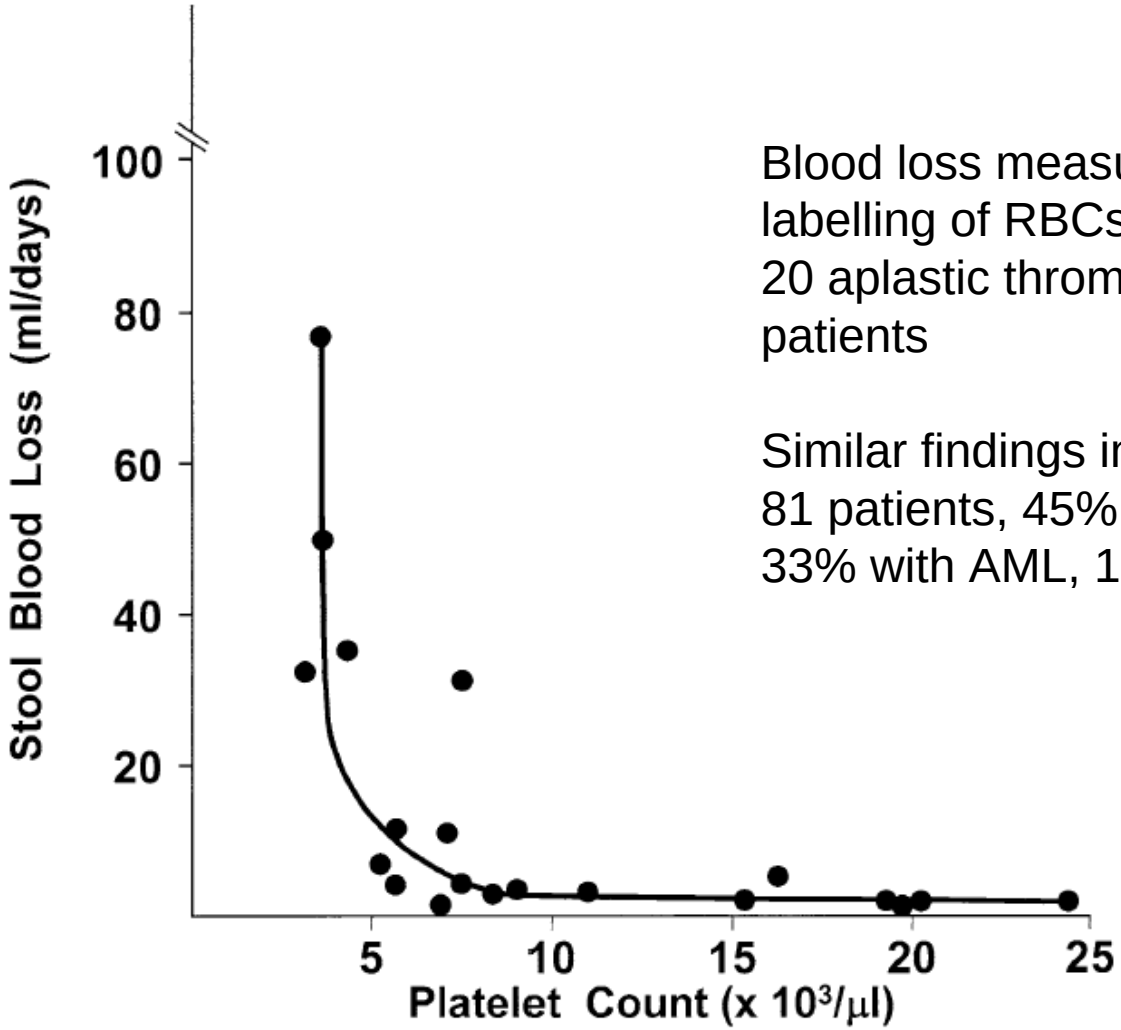
92 NCI patients
40 adults
52 children
34 AML
57 ALL

I = any bleeding
II = mod. bleeding
III = severe bleeding

Patients likely on aspirin

This is the study that formed basis for 20,000 trigger

How low can platelet counts get before patients bleed spontaneously? Slichter et al. (1978) Clin Haematol 7:523-539



Blood loss measured with Cr51 labelling of RBCs detected in stool of 20 aplastic thrombocytopenic patients

Similar findings in followup study of 81 patients, 45% with breast ca., 33% with AML, 11% with NHL

Data supporting the use of the 10,000/ul platelet count threshold for prophylactic platelet transfusions

Table 4. Summary of the Design, Platelet Dose and Outcomes in Studies of Thresholds for Prophylactic Platelet Transfusions

Study	Study Design (Level of Evidence)	n	PLT Dose	PLT Transfusion Threshold ($\times 10^9$/L)	1° Outcome
Gmur 1991[23]	Prosp Cohort (level IV)	105	1 SAP	5-20	No Δ in major bleeds
Fanning 1995[24]	Retro Cohort (level IV)	46	10 WBPU	10 or 20	No Δ in all bleeds
Gill-Fernandez 1996[25]	Retro Cohort (level IV)	191	1 WBPU/10 kg or 6 WBPU	10 or 20	No Δ in major bleeds
Heckman 1997[27]	RCT (level II)	78	1 SAP	10 or 20	No Δ in all bleeds
Rebulla 1997[28]	RCT (level I)	255	1 WBPU/10 kg or 1 SAP	10 or 20	No Δ in major bleeds
Navarro 1998[26]	Retro Cohort (level IV)	48	1 WBPU/10 kg	10 or 20	No Δ in major bleeds
Wandt 1998[29]	Concurrent cohorts (level III)	105	4-6 WBPU or 1 SAP	10 or 20	No Δ in major bleeds
Lawrence 2001[47]	Prosp Cohort (level IV)	141	5 WBPU or 1 SAP	10 or 20	No Δ in major bleeds

Abbreviations: Δ, change; Prosp, prospective; Retro, retrospective; SAP, single-donor apheresis platelet; WBPU, whole-blood–derived platelet unit.

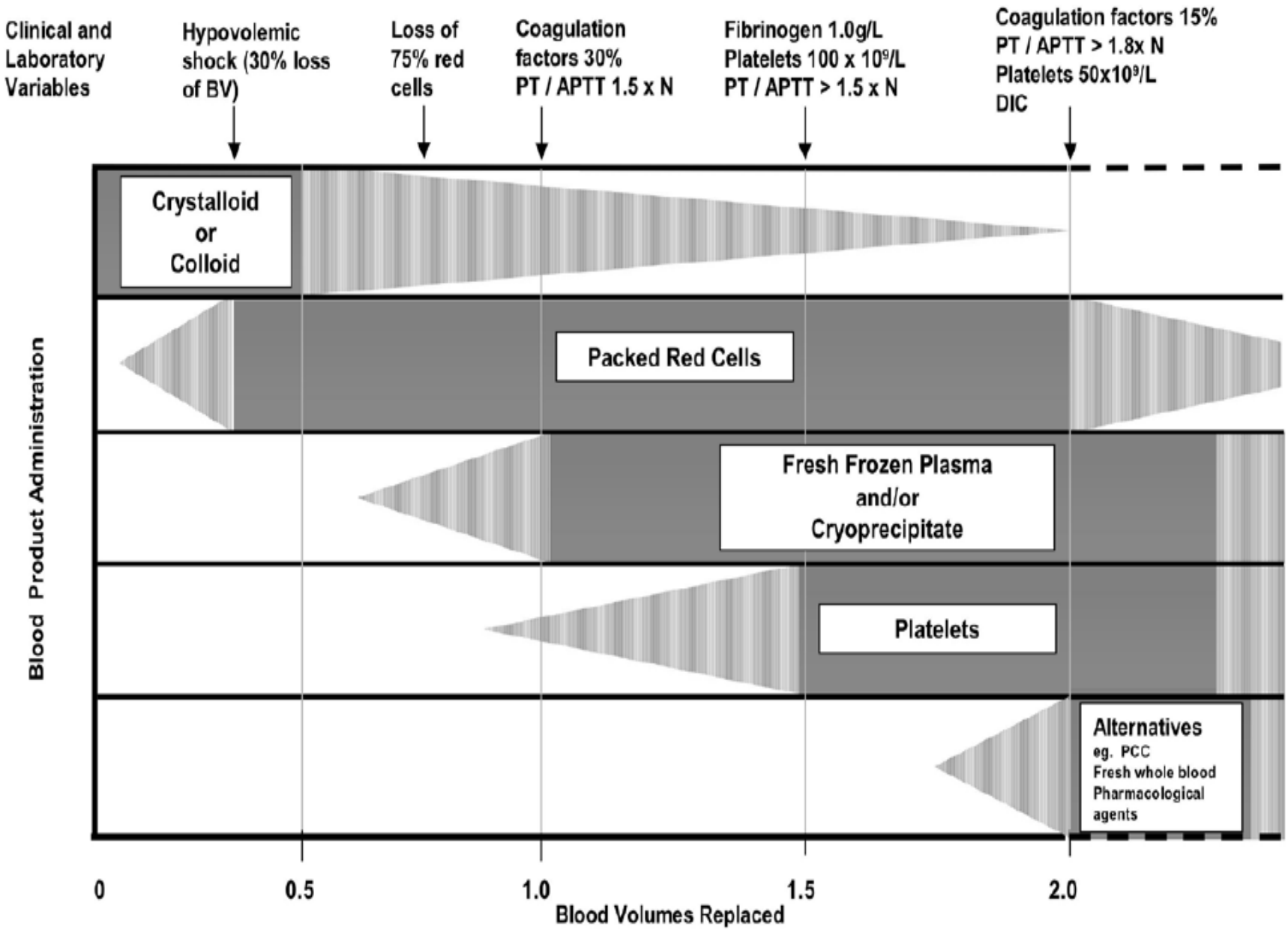
From Tinmouth and Freedman (2003)

Platelet transfusion triggers for lumbar punctures

- ASCO guidelines recommend having PLT count 20K or above based on studies of Edelson et al (1974) and Breuer et al (1982)
- Howard et al. (2000) JAMA 284: 2222-224:
  - No complications with 941 LP's performed in children with acute leukemia with platelet counts < 50K
  - 170 of these LP's performed at platelet counts of 10 to 20K
  - Similar findings by van der Veen et al. (2004)
- Risk of bleeding is believed to be greater with epidural placement or use of anticoagulant therapy but data is controversial

Platelet transfusion triggers for liver biopsies

- Wallace et al (2003)- Successful transjugular procedures with platelet counts < 30K
- McVay and Toy (1990)- No difference in rate of bleed complications associated with platelet counts > 50K versus normal platelet counts for percutaneous procedures



Hardy et al. Can J Anesth. 2004;51:303

What to do when a patient is platelet refractory and is unable to achieve desired platelet count with multiple transfusions

- Increasing dose escalations of platelet transfusions may increase donor exposure and development of HLA antibodies with no therapeutic or prophylactic benefit
- Need to rule out platelet refractoriness due to HLA antibodies
- Other possible causes of refractoriness include hypersplenism, fever, and infection
- If necessary reserve use of platelet transfusion until immediately before and during an invasive procedure

Recommendations for platelet transfusion triggers

- PLT count < 10,000/ ul for stable patients with no active bleeding
- PLT count < 20,000/ ul for stable patients who are febrile or have additional coagulopathies (liver disease, aspirin)
- PLT count < 50,000/ ul for patients who are undergoing an invasive procedure
- PLT count < 70,000/ ul for patients with uncontrolled bleeding

Speiss et al. (2004) Transfusion 44:1143-1148
Like RBC transfusions, platelet transfusions may increase mortality

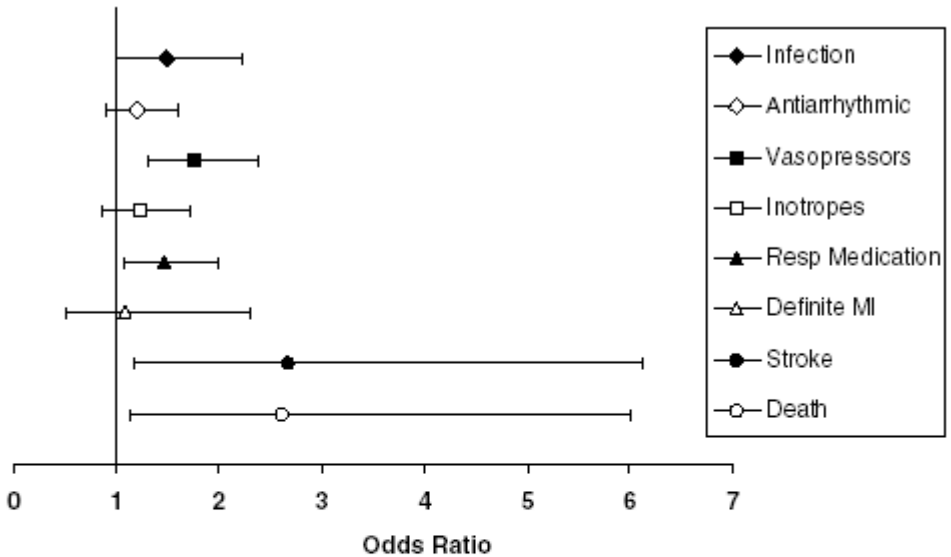


Fig. 2. Multivariate stepwise logistic regression analysis relating adverse outcomes to PLT administration in CABG patients. Data are not adjusted for administration of aprotinin. Association of PLT use and adverse outcomes are depicted with ORs (*x* axis) and 95-percent CIs (error bars). An OR greater than 1 indicates that PLT transfusion is associated with a higher rate of the adverse outcome. CIs that do not span 1 indicate that the association is significant.

- Data collected and analyzed retrospectively from 6 prospective randomized trials on the efficacy of aprotinin during cardiac surgery
- 1,720 patients from 37 medical centers
- Study may be flawed due to substantial differences in transfused and non-transfused patients
- Unlike for RBC transfusions, a prospective randomized clinical trial is currently lacking to fully address this question

Mangano et al. (2002) NEJM 347:1309-1317

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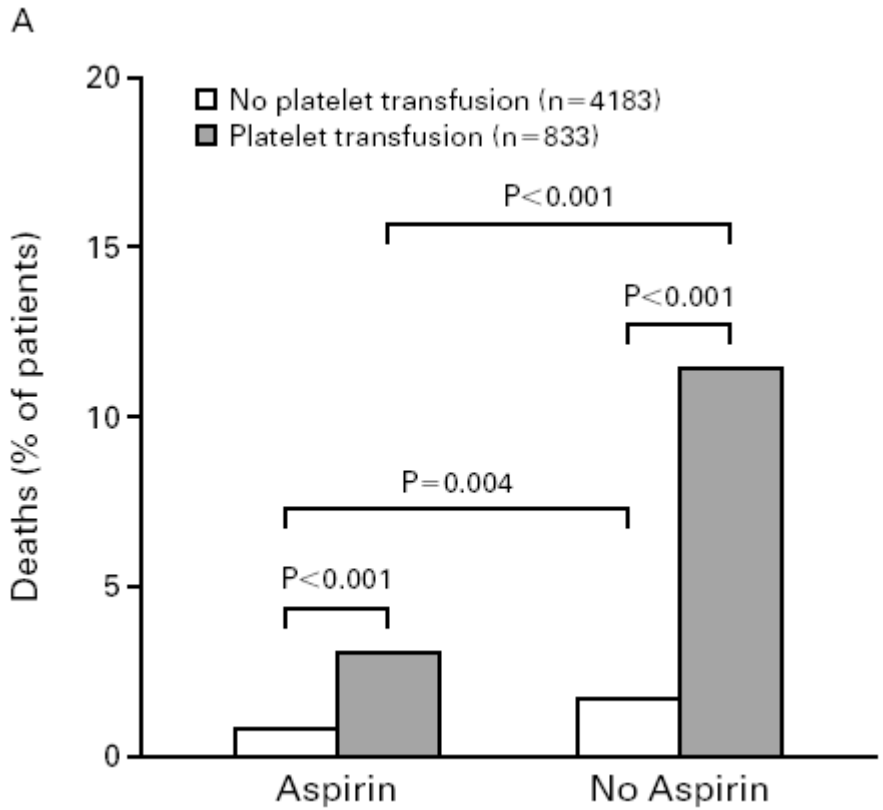

- Prospective, longitudinal study of 5436 patients at 70 medical centers with CAD undergoing CABG surgery
- Approximately 7500 variables measured

Lowered Hct decreases platelet aggregate formation on damaged endothelial surfaces

Escolar G et al. 1988 and 1994

Topical hemostasis

- Fibrin sealants
  - combination of purified thrombin and cryoprecipitate (aprotinin +$CaCl_2$)
  - reproduces the last stages of the coagulation cascade – conversion of fibrinogen into fibrin monomers and crosslinking of them into an insoluble fibrin matrix
- Platelet gel
  - mixture of a high concentration of autologous activated platelets in a small volume of plasma, thrombin and WBC
  - promotes wound healing

Hemostatic agents

- DDAVP:
  - synthetic vasopressin derivative, plasma levels of FVIII and vWF; directly increasing plt adhesiveness and improving primary hemostasis
  - may benefit management of acquired plt function defects
  - repeated administration leads to tachyphilaxis
  - antidiuretic hormone effect may lead to fluid retention and hyponatremia
- Vit K:
  - useful in prevention/treatment deficiency or oral anticoagulation
  - sq or im not as predictible as IV;rapid IV infusion(1 mg/min) associated w/ anaphylactic reactions
  - common approach 1-5mg. 1mg/hr by continuous infusion, correction takes about 6-8 hours

Hemostatic agents

- Antifibrinolytic agents: EACA, TA, aprotinin
  - EACA/TA: lysine analogs, inhibit fibrinolysis by binding to plasminogen and preventing its binding to the fibrin
  - Aprotinin: protease inhibitor, directly inactivates plasmin, preventing fibrinolysis
  - All effective in decreasing blood loss associated with CBP surgery
- Conjugated estrogens: promote primary hemostasis
- Erythropoietin: in CRF, resultant HCT increase improves in vivo platelet function

Summary

- Transfusions of platelets is associated with risks, infectious and non-infectious
- Likewise, the decision to not transfuse platelets may be associated with mortality or morbidity
- Evidence in the literature suggests that risks associated with not transfusing are often associated with platelet values far lower than commonly used transfusion triggers
- Decisions to transfuse platelets require some contemplation on the actual need of the patient vs. the potential risks