

New York State Council on Human Blood and Transfusion Services

***GUIDELINES FOR THE
ADMINISTRATION OF PLATELETS***

**Second Edition
2006**

**New York State Council on Human Blood and Transfusion Services
New York State Department of Health
Wadsworth Center
Empire State Plaza – P.O. Box 509
Albany, New York 12201-0509**

Second Edition 2006, First Edition 1994

Requests for copies of this publication may be directed to:

Blood and Tissue Resources Program
New York State Department of Health
Wadsworth Center
Empire State Plaza
P.O. Box 509
Albany, New York 12201-0509

Phone: (518) 485-5341

Fax: (518) 485-5342

E-mail: BTRAXESS@health.state.ny.us
www.wadsworth.org/labcert/blood_tissue

**NEW YORK STATE
COUNCIL ON HUMAN BLOOD AND TRANSFUSION SERVICES**

Membership Roster - 2006

Dennis Galanakis, M.D., Chairperson
Director, Blood Bank
SUNY Health Science Center at
Stony Brook
Stony Brook, New York

Robert A. Dracker, M.D., M.H.A.
Medical Director
Summerwood Pediatrics, and
Infusacare Medical Services
Liverpool, New York

William Fricke, M.D.
Director, Transfusion Service
Director, Hematology Laboratory
Rochester General Hospital
Rochester, New York

Alicia E. Gomensoro, M.D.
Director, Blood Bank
Maimonides Medical Center
Brooklyn, New York

Gloria Rochester
President
Queens Sickle Cell Advocacy Network
St. Albans, New York

Lazaro Rosales, M.D.
Director, Blood Bank
SUNY Health Science Center at Syracuse
Syracuse, New York

Donna Skerrett, M.D.
Director, Transfusion Medicine and
Cellular Therapy
New York Presbyterian Hospital -
Weill Cornell Medical Center
New York, New York

David Wuest, M.D.
Director, Blood Bank and Transfusion
Service
Memorial Sloan-Kettering Cancer Center
New York, New York

Antonia C. Novello, M.D., M.P.H., Dr.P.H.
(Ex-officio)
Commissioner
New York State Department of Health
Albany, New York

Jeanne V. Linden, M.D., M.P.H.
Executive Secretary
Director, Blood and Tissue Resources
New York State Department of Health
Wadsworth Center
Albany, New York

**NEW YORK STATE
COUNCIL ON HUMAN BLOOD AND TRANSFUSION SERVICES**

BLOOD SERVICES COMMITTEE

Membership Roster - 2006

Lazaro Rosales, M.D., Chairperson
Director, Blood Bank
SUNY Health Science Center at Syracuse
Syracuse, New York

Visalam Chandrasekaran, M.D.
Director of Medical Education
New York Blood Center
New York, New York

William Fricke, M.D.[†]
Director, Transfusion Service
Director, Hematology Laboratory
Rochester General Hospital
Rochester, New York

Elizabeth S. Gloster, M.D.^{*}
Director, Blood Bank
Kings County Hospital Center, and
SUNY Health Science Center at Brooklyn
Brooklyn, New York

Kathleen Grima, M.D.
Director, Clinical Services
New York Blood Center
White Plains, New York

Joanna Heal, M.D.
Associate Medical Director
American Red Cross Blood Services
West Henrietta, New York

Jeanne Linden, M.D., M.P.H.
Director, Blood and Tissue Resources
New York State Department of Health
Wadsworth Center
Albany, New York

Helen Richards, M.D.^{*}
Director of Laboratories
Harlem Hospital Center
New York, New York

Joan Uehlinger, M.D.
Director, Blood Bank
Montefiore Medical Center
Bronx, New York

David Wuest, M.D.
Director, Blood Bank and Transfusion
Service
Memorial Sloan-Kettering Cancer Center
New York, New York

[†] Guideline Working Group Chairperson

^{*} Member, Guideline Working Group

Table of Contents

Introduction	1
Rationale for Platelet Transfusion	1
Adverse Reactions to Platelet Transfusion	3
Indications for Platelet Transfusion	4
Pertinent Literature	6
General References	6
Reactions to Platelet Transfusion	6
Thrombocytopenia	7
Platelets and Bleeding	7
Alloimmunization	8

**NEW YORK STATE
COUNCIL ON HUMAN BLOOD AND TRANSFUSION SERVICES**

GUIDELINES FOR THE ADMINISTRATION OF PLATELETS

INTRODUCTION

The following guidelines are intended to provide general information about platelet transfusion. Platelets for transfusion are available in two forms: pools of platelet concentrates, and apheresis platelets in single or double units. Platelet concentrates are prepared from units of donated whole blood, separated within eight hours of collection, and contain a minimum of 5.5×10^{10} platelets. The usual quantity transfused to adults is a pool of five or six units, containing a total of 250 to 300 mL of plasma. Individual platelet concentrate units, which contain 40 to 50 mL of plasma, may be used for infants or small children. Apheresis platelets are collected from a single donor and contain a minimum of 3×10^{11} platelets (approximately equivalent to five or six platelet concentrate units) suspended in 200 to 300 mL of plasma.

In adults, a pool of five or six platelet concentrates, or a single apheresis unit should achieve a clinically meaningful increase in circulating, functioning platelets. A corrected count increment (CCI) of $>7,500$ (see page 3) or a platelet count increase of approximately 5,000 to 10,000/ μL per platelet concentrate unit administered is considered an acceptable response. If the increment observed is significantly lower than expected, in the absence of infection, splenomegaly, active bleeding, autoimmune thrombocytopenia, or other circumstances associated with platelet destruction, the patient may be alloimmunized to human leukocyte antigen (HLA) or platelet antigens. Patients who are refractory to platelet transfusions because of alloimmunization may benefit from HLA-matched or crossmatch-compatible platelets. Transfused platelets have been found to survive four to five days when returned to healthy subjects. However, because 7,000 to 10,000 platelets/ μL are consumed daily in plugging endothelial gaps, platelet survival in thrombocytopenic patients is reduced.

I. RATIONALE FOR PLATELET TRANSFUSION

Patients who may benefit from platelet transfusion include those with thrombocytopenia (hereditary or acquired) or platelet function disorders (hereditary or acquired). In either situation, platelet transfusions may be prophylactic or therapeutic. Prophylactic platelet transfusions are typically administered prior to an invasive procedure to patients at significant risk for platelet-related bleeding or to patients with severe thrombocytopenia who are at risk for spontaneous bleeding. Patients with autoimmune thrombocytopenia should receive platelets only in case of life-threatening bleeding. Therapeutic platelet transfusions are administered to patients who are bleeding due, at least in part, to either thrombocytopenia or platelet dysfunction. The guidelines below set forth more specific criteria. However, applying the guidelines strictly to individual patients may not always be appropriate. Before a transfusion is ordered, patients should be assessed to determine the likely benefit. The assessment should include determination of the current platelet count, evaluation of any bleeding to determine the likelihood that it is platelet-related, and consideration of any concurrent conditions that may increase the risk of such bleeding.

Several issues in this area are controversial. These include: the platelet count below which spontaneous bleeding is likely to occur (the so-called "threshold"); the degree of platelet

dysfunction, or number of dysfunctional platelets that increase the risk or extent of bleeding significantly; appropriate alternatives to platelet transfusion; and possible indications for using pooled platelet concentrates versus apheresis platelets.

Most hematologists and transfusion medicine specialists now agree that stable patients generally do not develop significant spontaneous bleeding until the platelet count falls below 5,000/ μ L. Other factors, such as coexisting coagulopathy, infection, other comorbidities, and certain medications, may increase the likelihood of bleeding; such high-risk patients should be maintained at higher platelet counts with prophylactic transfusions. The threshold platelet count for thrombocytopenic patients who are to undergo an invasive procedure is less clear. A common practice is to raise the platelet count to at least 50,000/ μ L, except for procedures involving the central nervous system or eye, for which the count is often increased to at least 100,000/ μ L. The validity of these numbers is unclear, since few data on this subject are available. Nonetheless, they are generally considered as adequate platelet counts for most procedures.

More problematic is the effect of antiplatelet drugs on the risk of bleeding. For instance, aspirin increases the bleeding time in most patients, although usually not beyond the upper limit of normal. In theory, this should increase the incidence of bleeding, but in practice, that does not appear to be the case, at least in stable patients with no other bleeding risk factors. Desmopressin acetate improves platelet function in such cases, and platelets are almost never indicated. Drugs such as clopidogrel, abciximab, and other platelet receptor blockers increase the risk of bleeding. Understanding the mechanism of action and pharmacokinetics of specific antiplatelet drugs may guide treatment options. Approximately 10 percent of circulating platelets are replaced every day, so even if all platelets were completely inactivated by a drug, numbers of functional platelets sufficient for hemostasis should be attained in only a few days after the last drug dose. Patients who are bleeding, and have recently taken one or more of these drugs, may need platelet transfusions.

Generally, nonbleeding patients may be treated more conservatively. Alternatives to platelet transfusion should be considered whenever possible. Antifibrinolytic drugs, such as epsilon aminocaproic acid (EACA) and tranexamic acid (TA), appear to lessen bleeding in some thrombocytopenic patients, as does desmopressin acetate. Aprotinin has also been given to some surgical patients who have been treated with antiplatelet drugs. Recombinant factor VIIa (rFVIIa) has been used with some success, but additional studies are needed to determine its usefulness definitively.

There are no specific indications for using apheresis platelets rather than pooled platelet concentrates. The extremely low prevalence of infectious diseases in the donor population makes it unlikely that pooled platelet concentrates would pose a significantly greater risk than do apheresis platelets. Previously, pooled platelet concentrates may have carried a higher risk of bacterial contamination than apheresis platelets, but the current American Association of Blood Banks (AABB) and College of American Pathologists (CAP) requirement that all platelets be tested for bacterial contamination is thought to have reduced this difference. Routine leukoreduction has diminished the likelihood of immunization to HLA or platelet-specific antigens, and apheresis platelets are considered equivalent to pooled platelet concentrates in alloimmunization risk. Many transfusion services provide mostly apheresis platelets because of their ease of preparation and handling.

Development of platelet refractoriness due to alloimmunization to HLA or platelet-specific antigens is an inherent risk for patients on chronic platelet transfusion therapy. If it develops, refractoriness typically does so within weeks of the first transfusion. The response to platelet transfusions should be monitored by obtaining a platelet count 10 to 60 minutes after each transfusion. Poor post-transfusion platelet count increments on at least two occasions suggest platelet refractoriness. *In vitro* demonstration of platelet antibodies (HLA antibodies or platelet-specific antibodies, or both) confirms the diagnosis. Once a patient is alloimmunized, subsequent unselected platelet transfusions are unlikely to be beneficial.

Care of an alloimmunized patient is challenging. HLA or platelet-specific antibodies should be identified to facilitate provision of HLA-matched and/or crossmatch-compatible platelets for transfusion. Platelets carry ABO antigens on their surface, and ABO-matched platelets have been found to survive better than those that are ABO-incompatible with the recipient's plasma. Unfortunately, neither HLA compatibility nor platelet-crossmatch compatibility is a guarantee of a good post-transfusion increment or of platelet hemostatic effectiveness in any given alloimmunized patient. The benefit of platelet transfusion in patients who do not exhibit an increase in platelet count is doubtful.

Whenever no other option is available for the severely thrombocytopenic, actively bleeding patient who is refractory to the usual doses of platelets, a constant or intermittent platelet infusion may be attempted. A maximum of one platelet concentrate unit per hour may be administered to adults, with up to four units being released at one time.

The clinical difficulty of caring for patients who have become refractory to platelets has prompted the development of preventive strategies. Leukoreduced blood components have been the option most frequently employed in the U.S. and are now routine. This technique reduces exposure to the leukocyte-associated HLA antigens thought to be responsible for inducing HLA alloimmunization.

Calculation of corrected count increment:

$$CCI = \frac{(\text{posttransfusion count} - \text{pretransfusion count}) \times \text{body surface area (M}^2\text{)}}{\text{platelets given} \times 10^{11}}$$

One unit of platelet concentrate should contain a minimum of 5.5×10^{10} platelets, and one unit of apheresis platelets, a minimum of 3.0×10^{11} platelets. The exact platelet count of the transfused component should be used for calculating CCI to assess alloimmunization.

II. ADVERSE REACTIONS TO PLATELET TRANSFUSION

Reactions to platelet transfusions are similar to those associated with other blood components. The risk of allergic reactions and of transmission of transfusion-associated viral diseases, such as hepatitis B and C, and HIV, are likely the same as for other cellular and plasma containing components. Febrile, nonhemolytic reactions following platelet transfusion are estimated to occur several times more frequently than following red cell transfusion. This is attributed to storage of platelets at room temperature (20 to 24 degrees Celsius), during which various biologic response modifiers, such as cytokines, may accumulate in the plasma. Platelets also pose a greater risk of bacterial contamination than do other blood components because of their room temperature storage. For this reason, the AABB and CAP require testing of all platelet components prior to transfusion. Finally, a

small number of red cells may be present in platelet components and may sensitize recipients to red cell antigens, primarily the D antigen. Therefore, Rh-negative patients who must receive platelets from Rh-positive donors should be considered for administration of Rh immune globulin, especially if the recipient is a female of childbearing potential.

Development of a positive direct antiglobulin test and/or hemolysis has been reported in cases in which group O platelets with high titer IgG ABO antibodies have been transfused to patients of other ABO types. For children and infants, the plasma of platelet components should be ABO-compatible with the recipient's red cells whenever possible.

III. INDICATIONS FOR PLATELET TRANSFUSION

A. Prophylaxis in patients with platelet counts $<10,000/\mu\text{L}$

Patients with platelet counts $\geq 5,000/\mu\text{L}$ who are not bleeding and are otherwise stable may not require transfusion. For counts from $10,000/\mu\text{L}$ to $20,000/\mu\text{L}$, clinical judgment must be exercised, with consideration of clinical circumstances that increase the risk of bleeding by compromising platelet function or survival. Aplastic patients are not usually transfused in the absence of serious bleeding.

Platelet transfusion is not indicated in cases of immune thrombocytopenia purpura (ITP) or post-transfusion purpura (PTP), unless the patient is bleeding. Such transfusion is contraindicated in thrombotic microangiopathies, such as thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS), in the absence of life-threatening bleeding. Platelet transfusions are also contraindicated in heparin-induced thrombocytopenia (HIT), because such transfusion may precipitate extensive intravascular coagulation.

B. Prophylaxis in patients with platelet counts $<50,000/\mu\text{L}$ prior to an invasive procedure

If surgery cannot be postponed, patients with platelet counts of $< 50,000/\mu\text{L}$ may require platelet transfusion. A platelet count of $> 100,000/\mu\text{L}$ is recommended for neurosurgical and ophthalmologic procedures.

For elective surgery, it is preferable to wait for the platelet count to rise either spontaneously or with appropriate treatment. In drug-induced and alcohol-induced thrombocytopenia, the platelet count usually returns to normal spontaneously within one to two weeks after the responsible agent has been withdrawn.

C. Active microvascular bleeding attributed to platelet dysfunction or thrombocytopenia

This group includes thrombocytopenic cardiac surgery patients with ongoing abnormal microvascular bleeding in whom no surgical cause can be identified. Such patients usually have qualitative platelet abnormalities believed to contribute to a bleeding tendency even if the platelet count is normal. Bleeding in patients with platelet counts $<50,000/\mu\text{L}$, including cardiopulmonary bypass patients, is platelet-related microvascular bleeding. Occasional patients, including cardiopulmonary bypass surgery patients, may develop platelet-related microvascular bleeding even when their platelet counts are greater than $100,000/\mu\text{L}$. However, prophylactic platelet transfusion is not indicated, given the absence of evidence of efficacy in preventing bleeding in cardiac surgery

patients. Prophylactic platelet administration after transfusion of a fixed number of red cell units is not indicated.

D. Intrinsic or acquired platelet dysfunction prior to an invasive procedure

Patients with platelet function disorders, whether hereditary or acquired, may respond to pharmacologic intervention with antifibrinolytics, desmopressin acetate, aprotinin, or rFVIIa. Unfortunately, none of the common assays, including the bleeding time test, platelet aggregation tests, PFA-100, and other platelet function tests, has been shown to correlate with clinical bleeding. Abnormal results on such tests, alone, do not constitute sufficient justification for platelet transfusion.

Acquired reversible platelet dysfunction occurs commonly in patients with renal insufficiency. In such patients, dialysis (in the case of frank uremia), desmopressin acetate, administration of erythropoietin or transfusion to reach a hematocrit of 30 percent, or estrogen may be employed as therapeutic strategies for bleeding. Cryoprecipitate may be effective in some patients if desmopressin acetate is unavailable, ineffective, or contraindicated. Platelet transfusion is not considered useful because transfused platelets are also affected by the uremia.

In patients with drug-induced platelet dysfunction, the responsible drug should be discontinued prior to elective surgery. Approximately 10 percent of circulating platelets are replaced each day; thus, enough platelets for normal hemostasis should be present within a few days after the last dose.

In patients with irreversible platelet dysfunction, as seen in myeloproliferative disorders, effective treatment of the underlying disease usually helps to correct the bleeding diathesis. However, desmopressin acetate and/or platelet transfusion may be necessary in acute surgical situations or if the patient is bleeding despite other therapies.

Patients with congenital platelet dysfunction, such as Glanzmann's thrombasthenia, Bernard-Soulier syndrome, and storage pool disease, often have bleeding beginning at an early age and usually require platelet transfusions to treat severe bleeding. Platelet transfusions are never indicated as treatment for von Willebrand disease, but desmopressin acetate may be of use (see *Guidelines for the Administration of Cryoprecipitate*, 3rd edition, 2006, New York State Council on Human Blood and Transfusion Services).

PERTINENT LITERATURE

General References

Bolan CD, Klein HG. Transfusion medicine and pharmacologic aspects of hemostasis. In: Kitchens CS, Alving BM, Kessler CM, eds. Consultative hemostasis and thrombosis. Philadelphia: WB Saunders, 2002:395-417.

British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the use of platelet transfusions. *Br J Haematol* 2003;122:10-23.

College of American Pathologists. Practice parameter for the use of fresh-frozen plasma, cryoprecipitate, and platelets. *JAMA* 1994;271:777-81.

Consensus Conference. Platelet transfusion therapy. *JAMA* 1987;257:1777-80.

Lee EJ. Indications for platelet transfusion therapy. In: Kurtz SR, Brubaker DB, eds. Clinical decisions in platelet therapy. Bethesda: American Association of Blood Banks, 1992:31-43.

Murphy S. Guidelines for platelet transfusion (editorial). *JAMA* 1988;259:2453-4.

National Heart, Lung, and Blood Institute. Indications for the use of red blood cells, platelets, and fresh frozen plasma. Bethesda, MD: National Heart, Lung, and Blood Institute, 1991. (Transfusion Alert. National Blood Resource Education Program, NIH Publication no. 91-2974a).

Practice guidelines for blood component therapy: a report by the American Society of Anesthesiologists Task Force on Blood Component Therapy. *Anesthesiology* 1996;84:732-47.

Reactions to Platelet Transfusion

Aye MT, Palmer DS, Giulivi A, Hashemi S. Effect of filtration of platelet concentrates on the accumulation of cytokines and platelet release factors during storage. *Transfusion* 1995;35:117-24.

Enright H, Davis K, Gernsheimer T, et al. Factors influencing moderate to severe reactions to PLT transfusions: experience of the TRAP multicenter clinical trial. *Transfusion* 2003;43:1545-52.

Ferrara JL. The febrile platelet transfusion reaction: a cytokine shower. *Transfusion* 1995;35:89-90.

Heddle NM, Klama L, Singer J, et al. The role of the plasma from platelet concentrates in transfusion reactions. *N Engl J Med* 1994;331:625-8.

Muyllé L, Joos M, Wouters E, et al. Increased tumor necrosis factor alpha (TNF alpha), interleukin 1, and interleukin 6 (IL-6) levels in the plasma of stored platelet concentrates: relationship between TNF alpha and IL-6 levels and febrile transfusion reactions. *Transfusion* 1993;33:195-9.

Ness P, Braine H, King K, et al. Single-donor platelets reduce the risk of septic platelet transfusion reactions. *Transfusion* 2001;41:857-61.

Noris M, Remuzzi G. Uremic bleeding: closing the circle after 30 years of controversies? *Blood* 1999;94:2569-74.

Wagner SJ, Robinette D. Evaluation of swirling, pH, and glucose tests for the detection of bacterial contamination in platelet concentrates. *Transfusion* 1996;36:989-93.

Weiner RS, Kao KJ. Clinical and laboratory diagnosis of the refractory state. In: Kurtz SR, Brubaker DB, eds. Clinical decisions in platelet therapy. Bethesda: American Association of Blood Banks, 1992:73-82.

Werch JB, Mhaweck P, Stager CE, et al. Detecting bacteria in platelet concentrates by use of reagent strips. *Transfusion* 2002;42:1027-31.

Thrombocytopenia

Bartholomew JR, Salgia R, Bell WR. Control of bleeding in patients with immune and non-immune thrombocytopenia with aminocaproic acid. *Arch Intern Med* 1989;149:1959-61.

Beutler E. Platelet transfusions: the 20,000/ μ L trigger. *Blood* 1993;81:1411-3.

Brown SM. Management of the thrombocytopenic patient. *New York Blood Center Seminars in Transfusion Medicine*, October 1993.

Diedrich B, Remberger M, Shanwell A, et al. A prospective randomized trial of a prophylactic platelet transfusion trigger of 10×10^9 per L versus 30×10^9 per L in allogeneic hematopoietic progenitor cell transplant recipients. *Transfusion* 2005;45:1064-72.

Friedberg RC, Donnelly SF, Mintz PD. Independent roles for platelet crossmatching and HLA in the selection of platelets for alloimmunized patients. *Transfusion* 1994;34:215-20.

Gmür J, Burger J, Schanz U, et al. Safety of stringent prophylactic platelet transfusion policy for patients with acute leukaemia. *Lancet* 1991;338:1223-6.

Hanson SR, Slichter SJ. Platelet kinetics in patients with bone marrow hypoplasia: evidence for a fixed platelet requirement. *Blood* 1985;66:1105-9.

Heckman KD, Weiner GJ, Davis CS, et al. Randomized study of prophylactic platelet transfusion threshold during induction therapy for adult acute leukemia: 10,000/ μ L versus 20,000/ μ L. *J Clin Oncol* 1997;15:1143-0.

Heyman MR, Schiffer CA. Platelet transfusion for the cancer patient. *Semin Oncol* 1990;17:198-209.

Murphy S. A critical view of prophylactic platelet transfusion. In: Kurtz SR, Brubaker DB, eds. Clinical decisions in platelet therapy. Bethesda: American Association of Blood Banks, 1992:45-54.

Rebulla P, Finazzi G, Marangoni F, et al. The threshold for prophylactic platelet transfusions in adults with acute myeloid leukemia. *N Engl J Med* 1997;337:1870-5.

Veenhoven WA, van der Schans GS, Huiges W, et al. Pseudothrombocytopenia due to agglutinins. *Am J Clin Pathol* 1979;72:1005-8.

Zumberg MS, del Rosario ML, Nejame CF, et al. A prospective randomized trial of prophylactic platelet transfusion and bleeding incidence in hematopoietic stem cell transplant recipients: 10,000/ μ L versus 20,000/ μ L trigger. *Biol Blood Marrow Transplant* 2002;8:569-76.

Platelets and Bleeding

De Loughery T. Hemorrhagic and thrombotic disorders in the intensive care setting. In: Kitchens CS, Alving BM, Kessler CM, eds. Consultative hemostasis and thrombosis. Philadelphia: WB Saunders, 2000:493-513.

Goodnough LT, Johnston MF, Ramsey G, et al. Guidelines for transfusion support in patients undergoing coronary artery bypass grafting. *Ann Thorac Surg* 1990;50:675-83.

Lind SE. The bleeding time does not predict surgical bleeding. *Blood* 1991;77:2547-52.

Livio M, Mannucci PM, Viganò G, et al. Conjugated estrogens for the management of bleeding associated with renal failure. *N Engl J Med* 1986;315:731-5.

Mannucci PM. Hemostatic drugs. *N Engl J Med* 1998;339:245-53.

McVay PA, Toy PT. Lack of increased bleeding after liver biopsy in patients with mild hemostatic abnormalities. *Am J Clin Pathol* 1990;94:747-53.

McVay PA, Toy PT. Lack of increased bleeding after paracentesis and thoracentesis in patients with mild coagulation abnormalities. *Transfusion* 1991;31:164-71.

Noris M, Remuzzi G. Uremic bleeding: closing the circle after 30 years of controversies? *Blood* 1999;94:2569-74.

Rao AK. Disorders of platelet function. In: Kitchens CS, Alving BM, Kessler CM, eds. Consultative hemostasis and thrombosis. Philadelphia: WB Saunders, 2002:138-48.

Rodgers RP, Levin J. A critical reappraisal of the bleeding time. *Semin Thromb Hemost* 1990;16:1-20.

Weigert AL, Schafer AI. Uremic bleeding: pathogenesis and therapy. *Am J Med Sci* 1998;316:94-104.

Alloimmunization

Heddle NM, Blajchman MA. The leukodepletion of cellular blood products in the prevention of HLA-alloimmunization and refractoriness to allogeneic platelet transfusions. *Blood* 1995;85:603-6.

Kickler TS. The platelet transfusion refractory state: transfusion practices and clinical management. In: Kurtz SR, Brubaker DB, eds. Clinical decisions in platelet therapy. Bethesda: American Association of Blood Banks, 1992:87-104.

Kickler TS, Herman JH, eds. Current issues in platelet transfusion therapy and platelet alloimmunity. Bethesda: AABB Press, 1999.

Narvios A, Reddy V, Martinez F, Lichtiger B. Slow infusion of platelets: a possible alternative in the management of refractory thrombocytopenic patients. *Am J Hematol* 2005;79:80.

O'Connell B, Lee EJ, Schiffer CA. The value of 10-minute posttransfusion platelet counts. *Transfusion* 1988;28:66-7.

Seftel MD, Grow GH, Petraszko T, et al. Universal prestorage leukoreduction in Canada decreases platelet alloimmunization and refractoriness. *Blood* 2004;103:333-9.

The Trial to Reduce Alloimmunization to Platelets Study Group. Leukocyte reduction and ultraviolet B irradiation of platelets to prevent alloimmunization and refractoriness to platelet transfusions. *N Engl J Med* 1997;337:1861-9.