Summary and Conclusions of the Meeting

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In summarizing the presentations and discussions of this symposium, it would seem there is agreement that decisions regarding platelet transfusions for chronic thrombocytopenic patients should involve close cooperation between the clinicians caring for the patient and the staffs of transfusion medicine so that management of these patients can be carefully controlled by all those involved.

Prophylactic platelet transfusions in hypoplastic patients are still controversial, and there is no general agreement. It depends on additional bleeding risk factors and evidence for bleeding. A platelet count $< 10,000/\mu\text{l}$ is accepted for prophylactic transfusion.

There appears to be agreement that transfusion for spontaneous bleeding in hypoplastic patients is acceptable if the platelet count is below $20,000/\mu\text{l}$. There is no agreement, however, concerning the dose of platelets that should be transfused. It seems reasonable that in the event of severe bleeding, platelets should be replaced if the count drops below $50,000/\mu\text{l}$. Transfusions should be adapted to maintain values about this level. For traumatic and surgical bleeding, it may be necessary to keep the platelet count above a threshold of $50,000/\mu\text{l}$, perhaps even above $80,000/\mu\text{l}$, for at least 4 days. The most common approach to management of refractoriness is to transfuse with HLA-selected donors, if refractoriness is due to anti-HLA antibodies. If the mechanism of refractoriness is unknown, a high dose of random platelets could be substituted. What may be preferred, in the absence of anti-HLA antibodies, is a frequent low dose of random platelets. It should also be considered to increase the hematocrit through red-cell replacement, because primary hemostasis improves when the hematocrit is higher. There are also data showing that aminocaproic acid, a monoamino carboxylic acid whose primary action is thought to be inhibition of the activation of fibrinolysis, may be helpful. More recently, tranexaminic acid, a competitive inhibitor of plasminogen activation, is discussed as another antifibrinolytic agent which may also have some activity. There does not seem to be much evidence that immunosuppressive drugs are useful.

I would like to discuss again random- versus single-donor apheresis platelets. Platelet function could be impaired with apheresis platelets because of donor factors. If the donor had a genetic disorder, such as von Willebrand's disease, or had taken drugs, the function of all the platelets would be affected and the transfusion would have a reduced therapeutic efficacy. Conversely, in random-pooled platelets, if the function of one donor's platelets is poor, this is compensated by the pooling of several units.

Relative to platelet concentrate preparation, apheresis products are without a doubt better than the platelet concentrates produced on a random basis from whole blood. Apheresis is clearly a

more standardized and controlled process compared to separation from buffy coat or platelet-rich plasma. As Dr. Andreu has already indicated, we should get away from platelets produced from platelet-rich plasma because the platelets from buffy coats are without a doubt better. Single-donor apheresis platelets also show better storage behavior. They remain better function during storage because it is possible to collect a more standardized product. Collection of a standard platelet product by apheresis technology with a known range in platelet concentration and plasma volume and with a low content of erythrocytes and leukocytes should result in less qualitative dysfunction during storage. But I believe that storage of apheresis products should be discontinued. It is a waste of a good product to store it for 5 days, and it is especially inappropriate if HLA-selected apheresis platelets have been collected. Patient alloimmunization: The apheresis platelet product collected by 3rd-generation cell separators, even without leukocyte depletion, is superior to buffy-coat platelets. Therefore, we believe that there is no need for leukocyte depletion if these products are used. However, a word of caution is needed - erythrocyte spillovers can occur with concomitant leukocyte contamination. I believe, though it is not yet proven, that there is no need for leukocyte depletion of HLA-selected apheresis products. Risks of transmission of infectious agents are usually lower for single-donor apheresis platelets than for random platelets from buffy coats or platelet-rich plasma.

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The question of how many donors are required to support a 4-week period of marrow hypoplasia for patients can be addressed in general. About 8 apheresis platelet concentrates are needed for these patients. Every 3-5 days, these patients receive apheresis platelet concentrates. Two donors are usually sufficient for this protocol compared to at least 40 donors if you use buffy-coat platelets. And, transfusion therapy with stored platelets adds another variable in that more transfusions would be required, which, in turn, would lead to a greater exposure to donor antigens plus transmission of infection.

The economics of transfusion must also be considered. The costs for a pooled preparation of 5 buffy-coat platelets are about 250 DM. Apheresis platelet concentrates from a random donor cost 520 DM, or about twice the cost of the buffy-coat-pooled platelets. Platelets collected from an HLA-selected donor cost about 700 DM, but if the interval between transfusions is increased because of the improved platelet quality and donor compatibility, fewer transfusions will be required during the period of aplasia and cost-effectiveness can be achieved. The influence of leukocyte depletion, apheresis products, buffy coat products, the strategies for platelet transfusions are all subjects of great interest. For patients with chronic thrombo-cytopenia, it may be important to define transfusion strategies to manage transfusion refractoriness when it occurs. For some centers with the capacity, it may mean availability of platelet concentrates from a pool of HLA-selected donors for those patients with documented anti-HLA antibodies. Such strategies require HLA typing of the patient at the time of diagnosis as well as maintaining a donor pool of known HLA typing, so specific donors can be recruited for platelet donation when needed. Posttransfusion response, i.e., increments, should be measured in all patients. Then, under circumstances in which donor selection by HLA does not result in a successful transfusion, cross-match assays may be used. Regular anti-HLA antibody screening of the recipient may be needed, as well as close clinical monitoring for signs of hemorrhage and other risk factors to develop a successful transfusion strategy for each patient. This requires close cooperation between the clinician caring for the patient and the transfusion service, so that trans-

fusions can be planned in accordance with patient need. With such detailed planning, emergency situations that occur at night, on weekends, or holidays can be effectively managed. Current trends indicate an increase in the demand for platelets. It will be crucial to establish indications for transfusion and avoid circumstances in which platelet transfusions are not indicated.

Relative to the platelet products transfused, questions regarding apheresis platelets versus buffy-coat concentrates versus random-pooled concentrates, leukocyte depletion etc. continue to be addressed by the transfusion community. Leukocyte depletion by filtration of platelet concentrates, collection of leukocyte-depleted concentrates by apheresis procedures which have predicted outcomes, or inactivation by irradiation show evidence of being a very important strategy in transfusion therapy.

There may be patient populations for whom one particular product has advantages over the other. In Europe, there is an increased use of random platelet concentrates from buffy coats, while the trend in the United States is toward apheresis single-donor platelet concentrates. There is also an increased utilization of leukocyte-depleted platelet products for special patient populations. Donors of apheresis platelets must also gain our attention. Fears of adverse reactions are now decreased, and considerations about regulations of the frequency of donation are being reevaluated.

New developments should be considered in our transfusion strategies. These include 1) virus inactivation techniques, 2) peripheral blood stem cell transplant protocols may reduce the duration of thrombocytopenia and transfusion dependence and 3) the use of cytokines – i.e., thrombopoietin, to stimulate marrow production of platelets which may decrease the need for platelet transfusion. Whatever the future, though, it will be the interaction between clinicians and the transfusion medicine services that will promote strategies of platelet transfusions which will reduce, or eliminate, mortality in thrombocytopenic patients; this is our ultimate goal. Hemapheresis is the tool by which we establish transfusion medicine as a clinical speciality.