

## Department of Transfusion Medicine

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### General Summary

1. In 2013, a study group funded by a Health and Labor Science Research Grant was formed to develop guidelines for easily distinguishing between transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO). We (principal investigator Tasaki and colleagues) have summarized the 3-year study on the adverse respiratory events associated with blood transfusions. We hope that the new guidelines will be useful for performing the correct differential diagnosis of the signs and symptoms associated with TRALI and TACO, so that the appropriate therapy can be implemented.
2. We attempted to demonstrate that antileukocyte antibodies in donor blood products directly induce a respiratory disorder in the transfusion recipient. However, we did not find a significant association between adverse events and antileukocyte donor antibodies.
3. Two years have passed since we began our participation in a study group investigating the relationship between hematopoietic stem cell transfusion and adverse reactions. The investigation of adverse reactions in hematopoietic stem cell infusions is an ongoing prospective multicenter observational study. To date, the incidence of adverse reactions is almost 40%, based on data collected from 522 patients. A detailed analysis will be performed after data is collected from a total of 1,000 patients.
4. In 2015, we participated in 2 multicenter collaborative studies: (1) Evaluation of Mononuclear Cells Positive for CD34 Marker by Fixed RBC Method and (2) A Study of Appropriate Demand and Use of Blood Products by Information and Communication Technology.
5. The summaries of 2 studies performed by our department were presented at the annual meeting of the Japan Society of Transfusion Medicine and Cell Therapy. One presentation was entitled “The significance of using aliquots of blood products in pediatric transfusion” and involved a study that found that the importance of using aliquots of units of packed red blood cells for pediatric surgeries could not be evaluated, because all the aliquots of a unit were used during surgery. However, the transfusion of aliquots was useful for children in pediatric wards. Unnecessary transfusions and waste were avoided. The second presentation was entitled “Current situation and problems of harvesting peripheral blood stem cells from related donors in our hospital.” The safe harvest of stem cells from healthy allogeneic donors is a top priority. Assessing CD34 cell counts in harvested mononuclear cells the day before apheresis might prevent the unnecessary administration of granulocyte colony-stimulating factor and lighten the burden of donors.

### Research Activities

1. Although a worldwide standard, which was developed in 2004 in Toronto, Canada, is

commonly used to diagnose TRALI, no such standard exists for diagnosing TACO. In 2013, a study group was formed to perform a study to establish Guidelines for the Differential Diagnosis of the Signs and Symptoms Associated with TRALI and TACO and for the Treatment of TRALI and TACO, Considered to be Serious Problems of Blood Transfusion. The final guidelines were presented in the *Journal of the Japan Society of Transfusion Medicine and Cell Therapy* (46[3], 2016).

2. Antileukocyte antibodies are thought to be a cause of TRALI. Because the rate of positive findings is higher in female donors, especially parous women, male donor-derived plasma has mainly been used for transfusion, with a subsequent reduction in transfusion-related dyspnea. However, few prospective studies have confirmed the association between antileukocyte antibodies in blood products and respiratory disorders in transfusion recipients. Our data from 70 patients who received allogeneic platelet units containing antileukocyte antibodies also could not confirm a significant association between antileukocyte antibodies in blood products and respiratory disorders in transfusion recipients. Because of the lack of evidence and the low incidence of TRALI, we have concluded that preventing TRALI by transfusing male-derived plasma should be strongly recommended with a continued focus on the relationship between TRALI and antileukocyte antibodies. Our philosophy is similar to that used to prevent posttransfusion graft-versus-host disease, which is to irradiate units of allogeneic blood instead of focusing on assessing the similarities of the HLA profiles of blood donors and recipients.

3. Various adverse reactions, including nausea and fever, occur in patients who undergo hematopoietic stem cell transplantation (HSCT) and are probably due to the simultaneous transfusion of anticoagulant and cryoprotectant (dimethylsulfoxide). However, little information is available for preventing such reactions after HSCT. In 2015, Dr. Ohto (Fukushima Medical University) formed a study group of 20 investigators which began gathering detailed information on HSCT: the timing, duration, types, and severity of adverse events and the necessity of therapy. We provided data on 40 patients who underwent HSCT before December 31, 2015. The interim results indicate that adverse reactions occurred in a significantly higher percentage of patients undergoing allogeneic bone marrow transplantation (51.7%) than of patients undergoing autologous peripheral blood stem cell transplantation, (40.3%). Among the various adverse reactions, a change in blood pressure was the most significant. The target number of patients is 1,000.

4. CD34 is thought to be a surface marker of HSCs, and accurately quantifying HSCs in samples of mononuclear cells is important for HSCT. The principal investigator, Dr. Okuyama, and his colleagues (Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital) sent 2 different cell samples to 55 HSCT facilities for CD34 cell quantification. The results were collected and compared to the results measured with the gold-standard method. Each facility was graded; we received a grade of A for each sample.

5. Although allogeneic blood donation is safe, we have a responsibility to use blood products carefully and appropriately, especially for children with long life expectancies. From a practical perspective, the division of a unit of packed red cells (approximately 160 ml) into 2 to 3 aliquots seems sensible, because the amount of blood used at one time is small. However, because the shelf life of platelets is only 24 hours in Japan, the division of

platelet units into aliquots is not practical.

The 2013 approval in Japan of stem cells harvested from unrelated donors will increase the number of donors who will choose peripheral blood stem cell harvest.