

risk of VT and TS in children, and (2) the observed negative correlation of genetic VT risk with the plasma levels of the fibrinogen  $\gamma'$  variant suggests that FGG-H2 and -H3 haplotypes modify thrombosis risk by controlling the level of this FGG splice isoform.

In response to our manuscript, Cheung and coworkers note that elevated fibrinogen  $\gamma'$  ratios are associated with cardiovascular diseases and acute phase reaction but not with clinical outcome. This is an interesting observation regarding the use of  $\gamma'$  levels/ratios as a predictive biomarker for short-term clinical course. The authors tentatively explain this observation with altered mRNA processing of the fibrinogen  $\gamma'$  during an acute phase reaction. The data by Cheung and colleagues, however, should not be intermingled with the genetic issues that are subject of our publication.<sup>1</sup> As pointed out correctly by Cheung et al, in our cohort study blood samples for fibrinogen  $\gamma'$  investigation clearly have been drawn beyond the acute phase, 6 to 12 months after acute VT onset. Thus, on the bases that (1) none of the children investigated by us had evidence of acute phase reactions (underlined by normal values of high sensitive C-reactive protein, von Willebrand factor antigen [data not shown]), (2) missing nonacute fibrinogen  $\gamma'$  levels, and (3) missing fibrinogen haplotype associations in the cohort by Cheung and coworkers, both scientific reports cannot be directly compared. Whether fibrinogen  $\gamma'$  serves as a predictive biomarker for acute phase reaction, for short- or long-term clinical outcomes or both, should be addressed in future prospective studies.

**Ulrike Nowak-Göttl**

*Pediatric Hematology/Oncology,  
University of Muenster,  
Muenster, Germany*

**Hartmut Weiler**

*Blood Research Institute,  
Blood Center of Wisconsin,  
Milwaukee*

**Monika Stoll**

*Leibniz-Institute for Arteriosclerosis Research,  
Genetic Epidemiology of Vascular Disorders,  
Muenster, Germany*

**Contribution:** M.S. and U.N.-G. are the principal study investigators; H.W. performed the biochemical studies on fibrinogen  $\gamma'$  variants and contributed to data analysis; and all authors were responsible for writing the letter.

**Conflict-of-interest disclosure:** The authors declare no competing financial interests.

**Correspondence:** Monika Stoll, Leibniz Institute for Arteriosclerosis Research, Domagkstr 3, Muenster 48149, Germany; e-mail: mstoll@uni-muenster.de.

## Reference

1. Nowak-Göttl U, Weiler H, Hernandez I, et al. Fibrinogen alpha and gamma genes and factor V Leiden in children with thromboembolism: results from 2 family-based association studies. *Blood*. 2009;114(9):1947-1953.

## To the editor:

### Allogeneic transplantation for children and adolescents with Hodgkin lymphoma

Our article on allogeneic hematopoietic stem cell transplantation in children and adolescents with recurrent and refractory Hodgkin lymphoma<sup>1</sup> was accompanied by an Inside *Blood* commentary written by Dr James Nachman. Although we agree that registry data need special attention in order not to draw unjustified conclusions, we disagree with other conclusions not supported by any data and reject his “impression” that “the evidence that reduced-intensity conditioning (RIC) is associated with a higher relapse rate compared with myeloablative conditioning is flawed and should not be given significant credence.”

In fact, several papers on allogeneic transplantation for Hodgkin lymphoma<sup>2</sup> and other diseases<sup>3,4</sup> repeatedly demonstrated that RIC results in significantly increased relapse rates if compared with myeloablative conditioning (MAC). We maintain our conclusion that more vigorous (not necessarily fully myeloablative) conditioning is a viable option to reduce the high relapse rates seen in all patients receiving transplants for Hodgkin lymphoma. This may be particularly attractive in children and adolescents who tolerate aggressive chemotherapy as part of the conditioning regimen much better than older patients. The unique difference between children/adolescents and adult patients is that nonrelapse mortality (NRM) after MAC is high in adults, whereas this was not seen in children and adolescents.<sup>1</sup> To further substantiate this finding we reanalyzed NRM in our dataset but this time included all patients below the age of 21 years. Even in this still young population (n = 151) NRM after MAC was significantly higher than after RIC, whereas in our paper we reported that NRM curves were superimposable in 91 patients aged 18 years or younger who received RIC or MAC.

Another concern raised by Dr Nachman is based on the fact that approximately half of the patients reported by the European Group for Blood and Marrow Transplantation (EBMT) underwent allogeneic transplantation as their first transplantation. We do not have all the information available to describe fully the decision-making process in individual transplant centers. However, Dr Nachman and the reader should be aware that EBMT has been running the only prospective study on allogeneic transplantation for Hodgkin lymphoma (HD-R ALLO study; A.S., C. Canals, R. Arranz, D. Caballero, J. M. Ribera, M. Brune, J. Passweg, J. Besalduch, R. F. Duarte, A. Léon, M. J. Pascual, N.S., oral presentation submitted for 2009 ASH annual meeting), in which patients with refractory disease after first-line therapy or early first relapse could be included. Because of the discussions preceding this study and the poor results of autologous transplantation in chemorefractory patients, some clinicians obviously preferred an allogeneic over an autologous transplantation. To address the question of any potential bias introduced by analyzing patients who had not received an autologous transplant before allogeneic transplantation, we did a multivariate analysis and reported the results in our paper. Neither the number of previous lines of therapy nor a prior autologous transplantation influenced the relapse rates; one significant factor with a negative impact on relapse rate was RIC. Thus, we do not believe that our results are flawed by including patients who had not failed an autologous transplantation or by any other selection process. We do believe, however, that clinical decision-making should be guided by facts and not by “impressions” or “general consensus” as recommended

by Dr Nachman. We agree with Sigmund Freud, who stated in *Reflection on War and Death*: “Illusions commend themselves to us because they save us pain and allow us to enjoy pleasure instead. We must therefore accept it without complaint when they sometimes collide with a bit of reality against which they are dashed to pieces.”<sup>5</sup> Undoubtedly, RIC represents a major achievement in hematopoietic stem cell transplantation; however, we believe that a more sophisticated approach to conditioning, rather than “one size fits all,” is warranted.

**Norbert Schmitz**

*Hematology and Stem Cell Transplantation,  
Asklepios Klinik St Georg,  
Hamburg, Germany*

**Anna Sureda**

*Clinical Hematology Division,  
Hospital de la Santa Creu i Sant Pau,  
Barcelona, Spain*

**Giorgio Dini**

*Dipartimento di Ematologie ed Oncologia,  
Institute G. Gaslini,  
Genova, Italy*

**Alexander Claviez**

*Department of Pediatrics and Bone Marrow Transplant Unit,  
University Hospital Schleswig-Holstein,  
Kiel, Germany*

**on behalf of the Lymphoma and Pediatric Diseases Working Parties**

**Conflict-of-interest disclosure:** The authors declare no competing financial interests.

**Correspondence:** Prof Norbert Schmitz, Hematology and Stem Cell Transplantation, Asklepios Klinik St. Georg, 15 Lohmuehlenstr, 20099 Hamburg, Germany; e-mail: n.schmitz@asklepios.com.

## References

1. Claviez A, Canals C, Dierickx D, et al. Allogeneic hematopoietic stem cell transplantation in children and adolescents with recurrent and refractory Hodgkin lymphoma: an analysis of the European Group for Blood and Marrow Transplantation. *Blood*. 2009;114(10):2060-2067.
2. Sureda A, Robinson S, Canals C, et al. Reduced-intensity conditioning compared with conventional allogeneic stem-cell transplantation in relapsed or refractory Hodgkin's lymphoma: an analysis from the Lymphoma Working Party of the European Group for Blood and Marrow Transplantation. *J Clin Oncol*. 2008;26(3):455-462.
3. Crawley C, Iacobelli S, Björkstrand B, et al. Reduced-intensity conditioning for myeloma: lower nonrelapse mortality but higher relapse rates compared with myeloablative conditioning. *Blood*. 2007;109(8):3588-3594.
4. Ringdén O, Labopin M, Ehninger G, et al. Reduced intensity conditioning compared with myeloablative conditioning using unrelated donor transplants in patients with acute myeloid leukemia. *J Clin Oncol*. 2009;27(27):4570-4577.
5. Cited in Longo DL. The use of chemotherapy in the treatment of Hodgkin's disease. *Semin Oncol*. 1990;17(6):716-735.



**blood**<sup>®</sup>

2009 114: 4605-4606  
doi:10.1182/blood-2009-09-243766

## **Allogeneic transplantation for children and adolescents with Hodgkin lymphoma**

Norbert Schmitz, Anna Sureda, Giorgio Dini, Alexander Claviez and on behalf of the Lymphoma and Pediatric Diseases Working Parties

---

Updated information and services can be found at:  
<http://www.bloodjournal.org/content/114/20/4605.full.html>

Articles on similar topics can be found in the following Blood collections

---

Information about reproducing this article in parts or in its entirety may be found online at:  
[http://www.bloodjournal.org/site/misc/rights.xhtml#repub\\_requests](http://www.bloodjournal.org/site/misc/rights.xhtml#repub_requests)

Information about ordering reprints may be found online at:  
<http://www.bloodjournal.org/site/misc/rights.xhtml#reprints>

Information about subscriptions and ASH membership may be found online at:  
<http://www.bloodjournal.org/site/subscriptions/index.xhtml>