Conflict-of-interest disclosure: B.B. serves on research advisory boards for Celgene and Millennium corporations, and his institution has received data management support from both companies; J.D.S. serves on an advisory board for Novartis and has received honoraria from that company; the remaining author declares no competing financial interests.

REFERENCES

CLINICAL OBSERVATIONS

Comment on Neunert et al, page 4003

Childhood ITP: can we venture below 20 000?

Thomas Abshire  EMORY UNIVERSITY

In a large study of children with acute ITP published in this issue of Blood, Neunert and colleagues find that irrespective of therapy aimed at raising the platelet count or the severity of thrombocytopenia, severe bleeding is rare. Contrary to the exploits of Captain Nemo and his crew in Jules Verne’s epic novel, there have been few hearty souls willing to venture below the surface of conventional childhood acute immune thrombocytopenic purpura (ITP) management and ask whether symptoms, platelet count, and intervention at diagnosis could predict bleeding severity and incidence in the next month. Accordingly, controversy still exists regarding management of ITP in these children. Specifically, should treatment be administered at all, for whom, and with which drugs? Drug treatment of ITP is often used to prevent serious bleeding, and the initial platelet count is assumed to be a surrogate for bleeding potential, especially for those who present with minimal bleeding. By most accounts, life-threatening hemorrhage, especially intracranial or central nervous system (CNS) bleeding, is quite rare (approximately 1 in 800 cases; 0.125%). But clinical anxiety often creeps in when there is mild mucosal bleeding, and the platelet count is firmly below sea level (less than or equal to 20 000 per mm³). This study by Neunert et al is the first to prospectively chronicle the severity of hemorrhage at diagnosis and in the next 4 weeks, as well as the relationship of clinical symptoms to the platelet count and treatment intervention.

Eight hundred sixty-three of 1106 enrolled patients were fully evaluable, and the vast majority had no or mild bleeding at diagnosis and a platelet count of less than or equal to 20 000 per mm³. Therapy aimed at raising the platelet count was left to provider discretion. The table illustrates the distribution of various treatments for those presenting with no to mild bleeding symptoms and the number of patients (n = 3) with serious bleeding within the first month after diagnosis. Severe bleeding was defined as mucosal or CNS bleeding, requiring hospitalization and/or blood transfusions. All 3 patients had non-CNS bleeding. As expected, there was a significant difference between the platelet count and bleeding symptoms at diagnosis: mild bleeding equals 17 000/mm³, moderate equals 10 000/mm³, and severe equals 9000/mm³.3
However, there was no difference in subsequent severe bleeding in those with mild to moderate bleeding at diagnosis, whether or not treatment was given. Additionally, patients were more likely to receive treatment at diagnosis if their platelet count was low (range: 7000-12 000/mm³).

This investigation is important on several accounts. First, the prevalence of severe bleeding (including CNS) is similar to another large study (3%). Second, treatment did not statistically impact the development of severe bleeding by 4 weeks, even if the bleeding at diagnosis was moderate. Finally, similar to the findings from a prior study, treatment of major hemorrhage at diagnosis may not alter bleeding symptoms over the next several days. Words of caution regarding this study include a lack of validation of the bleeding score instrument and the inability to determine, by study design, the potential clinical benefits of judiciously raising the platelet count with drug intervention. As the authors suggest, serious bleeding in childhood acute ITP is quite rare, making design and completion of a definitive drug intervention trial that might show a difference in bleeding rates difficult. Accordingly, this author agrees with the investigators that subsequent studies in childhood ITP should be aimed at investigating quality of life (focusing on both treatment side effects/adverse events and the troublesome symptoms of bleeding without treatment), the cost of treatment, or identifying clinical or laboratory markers that may predict the development of severe bleeding during the first 28 days after diagnosis.

Even though there was a significant relationship at diagnosis between the platelet count and bleeding severity, the platelet count is not a good surrogate for treatment, as severe mucosal bleeding by itself would have dictated intervention. Also, even though most patients with a platelet count of less than or equal to 20 000/mm³ and mild to moderate bleeding symptoms did receive treatment at diagnosis, there was no statistical difference in subsequent development of new severe bleeding at 4 weeks. In fact, only 6 patients experienced this complication (4 with treatment and 2 without). Currently, most clinicians still use a platelet count of less than or equal to 20 000 to institute treatment, regardless of the severity of bleeding symptoms. The data in this paper, however, would support allowing platelet counts to dive below this level and to treat based on clinical bleeding severity, thus avoiding costly and sometimes toxic treatment for patients who have only mild to moderate clinical bleeding at presentation.

Conflict-of-interest disclosure: The author declares no competing financial interests.

REFERENCES

Comment on Bartman et al, page 3995

Hematologic hints of HTLV-2 in US blood donors

Mark A. Beilke MEDICAL COLLEGE OF WISCONSIN

The HOST investigators have maintained a multiregional and longitudinal survey of donors infected with HTLV-I and HTLV-II for over 14 years. The survey has provided extremely valuable information regarding the long-term consequences of asymptomatic infection with HTLV-I or HTLV-II. In this issue of Blood, Bartman and colleagues demonstrate an association with abnormalities in hematologic parameters among HTLV-I and HTLV-II–infected blood donors through time, including elevations in hemoglobin, mean corpuscular volume, platelet counts, and absolute lymphocyte counts. United States prior to the initiation of blood donor screening in 1988. Limited information exists regarding the long-term biologic and clinical outcomes of HTLV-II infection. Previous reports from the HTLV Outcomes Study (HOST) have linked HTLV-II infection with increased morbidity/mortality, an increased risk for pneumonia and bronchitis, urinary tract infections, and rare neurologic
 Childhood ITP: can we venture below 20 000?

Thomas Abshire