REFERENCES


Response

We thank Drs Escolar and White for their interest in our study reporting that a 50% reduction of platelet surface GPIb expression does not affect platelet adhesion. When we activate platelets in vitro, a reduced expression of GPIb on the platelet membrane was found, both using semiquantitative immuno electron microscopy (IEM) as well as FACS analysis. We have much experience in immunogold cytochemistry and we are aware of the pitfalls in quantifying gold particles. Indeed, a dilated open canalicular system (OCS) is better accessible to luminal antibodies than a narrow OCS. However, limited access is generally not a problem for antigens present on the cell surface. Because we found comparable results with both EM and FACS techniques, we are convinced that in vitro experiments GPIb expression on the surface is reduced. The impact of our article is that reduction of GPIb on the platelet surface does not influence platelet adhesion. It was not our aim to enter the endless discussion of whether GPIb expression on the cell surface is reduced or not.

At present, it is still unclear whether platelet activation in vivo results in diminished surface expression of GPIb. Unpublished studies performed in our laboratory during cardio-pulmonary bypass surgery did not show a reduced GPIb surface expression, which is in line with other studies that showed only a minor reduction. An interesting question is what happens with platelets of carriers of Bernard-Soulier syndrome when their platelets are activated and have lost 50% of the remaining GPIb on the cell surface. Obviously, the carriers do not bleed. There are two explanations for the lack of bleeding: the reduction of GPIb after activation only occurs in vitro and not in vivo or, as we have shown in our report, there is an immediate redistribution of GPIb after adhesion of the platelets, resulting in a restored GPIb expression on the platelet surface.

We agree that, in the case of fully spread platelets, most of the OCS membrane become part of the cell surface. The complete spreading of the platelets to which Drs Escolar and White refer is only achieved after 20 minutes of static adhesion to formvar and is never observed during a 5-minute perfusion over type III collagen, especially not when dRGDW is used to avoid platelet aggregation.

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TT Virus Viremia and Liver Transplantation: No Significant Increase of the Prevalence

To the Editor:

TT virus (TTV) is a novel DNA virus that has been assumed to be associated with posttransfusion hepatitis.1,2 A recent investigation showed that, in 28 of 200 healthy blood donors (14%), TTV viremia could be detected by polymerase chain reaction (PCR).3 To determine the risk for TTV transmission by blood and blood products, we examined 104 patients (39 women and 65 men; mean age, 49 years) who underwent liver transplantation (LTX) between 1992 and 1996 in a retrospective study. These patients are at high risk for acquiring transfusion transmitted agents due to the numerous units of blood and blood products administered during surgery. Seventeen of them (16.4%) had a history of fulminant hepatic failure (FHF) that was due to hepatitis B virus (HBV; n = 5), to hepatitis A virus (HAV; n = 1), or of unknown etiology (n = 11). The other 87 patients (83.7%) had liver cirrhosis due to autoimmune hepatitis (n = 24), chronic hepatitis C virus (HCV) infection (n = 27), chronic HBV infection (n = 11), HBV and hepatitis D virus (HDV) infection (n = 4), alcohol abuse (n = 15), or unknown etiology (n = 6).

TTV infection was investigated by nested polymerase chain reaction (PCR) using primers of a conserved region within the postulated open reading frame 1.2 Before liver transplantation, TTV DNA was detectable in 18 (17.3%) of the 104 patients. The titters of TTV viremia were determined by serial dilution and the median value was 2 × 10³
copies/mL. Of these 18 patients, 5 had autoimmune hepatitis, 4 were infected with HBV, 1 was infected with HBV and HDV, 5 were infected with HCV, and 1 was an alcoholic. Two of the TTV PCR-positive patients had HFH of unknown etiology. However, in the remaining 9 patients with HFH of unknown etiology, no TTV viremia was detectable. Postoperatively, the 18 initially and 7 additionally TTV viremic patients had detectable viremia in sera drawn between days 6 and 14 after transplantation. On follow-up, 5 viremic patients showed a persistent viremia for at least 18 months.

Because transfusion of blood and blood products is supposed to be a major route of TTV transmission, 1,4 we examined the number of blood products (blood plasma and erythrocyte and thrombocyte concentrates) administered to the patients in connection with the LTX. There was no significant difference between the number of blood products administered to the patients who became TTV PCR-positive postoperatively (median, 108 U) and the patients who remained TTV PCR-negative (median, 140 U).

Although each patient had received a great number of blood products, our data demonstrate that the prevalence of TTV viremia did not significantly increase from 17.3% to 24% during LTX. This finding is in sharp contrast to GBV-C/HGV, where in the identical collective of patients an increase of the prevalence from 6% before to 41% after transplantation was observed, as recently described. 5 The prevalence of TTV viremia in healthy blood donors was shown to vary from 1.5% to 14%. 2,4 Thus, each patient must have received 2 to 20 TTV-positive units of blood products. One reason for the unexpected low increase of TTV prevalence in the recipients might be due to the presence of protective antibodies in the majority of the patients. This will be clarified as soon as serological assays for the detection of TTV antibodies are available. Furthermore, we conclude from our data that TTV infection is not linked to fulminant hepatic failure, because the prevalence in this group of patients does not exceed the prevalence in German and Japanese blood donors. 2,3 Clinical studies are currently in progress to evaluate the clinical impact of TTV infection in liver transplant recipients.

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Quality Issue: Marrow Interpretations

To the Editor:

In the past, hematologists/oncologists performed bone marrows and often forwarded clot and biopsy material (in some instances, aspirate samples as well) to local laboratories. In this manner, the hematologist/oncologist was able to review the slides personally or with the pathologist. This process permitted the correlation of clinical and pathologic information and allowed for more accurate diagnoses upon which treatment decisions were made. The time for this entire process was brief (several days).

In the current cost conscious climate, insurance companies and managed care organizations arrange the processing of pathology samples and subsequent interpretations by reference laboratories. Oftentimes, these laboratories are no longer next door, nor are the clinicians able to relate personally with slides or pathologists. We decided to measure the accuracy and timeliness of bone marrow samples (performed in our outpatient clinic) that were forwarded to reference laboratories.

Bone marrow clot and biopsy samples obtained on 28 patients over 6 months at the Baptist Regional Cancer Center were logged for rapidity of returned reports, frequency of returned slides, and accuracy of pathology interpretation (Table 1). In each case, a request was made for slides to be returned for personal review. Four reference laboratories were used, as noted by anonymous letter code. Bone marrow verbal or written reports were received at a median of 9 days (range, 2 to 28 days). Only 11 of 28 (39%) requests resulted in returned slides; median time for receipt of slides was 21 days. I personally reviewed all returned slides; however, when disagreement occurred, I asked one of our next-door pathologists to re-review the slides in an impartial manner without indicating I was assessing a potential quality issue. Errors were noted in 5 of the 11 (45%) cases. No attempt was made to assess

<table>
<thead>
<tr>
<th>Table 1. Marrows Sent to Reference Laboratories</th>
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<tbody>
<tr>
<td>1. No. of samples forwarded: 28</td>
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<tr>
<td>2. Reference laboratories Errors</td>
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<tr>
<td>A. 20</td>
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<td>B. 4</td>
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<td>C. 3</td>
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<td>D. 1</td>
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<td>3. Length of time for report: 9 days (median)</td>
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<td>2-28 days (range)</td>
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<td>4. Slides returned for review: 11 of 28 (39%)</td>
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<td>5. Time for appearance of slides (of those returned): 21 days (median)</td>
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<td>6. Interpretation disagreement: 5 of 11 (45%)</td>
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