Transfusion-transmitted virus (TTV) is a newly described nonenveloped, single-stranded DNA virus, recently detected with high prevalence in Japanese patients with fulminant hepatitis and chronic liver disease of unknown origin. Having a high buoyant density (1.26 g/mL) and very low density (1.15 g/mL) in gradient centrifugation, single-stranded DNA virus, recently detected with high prevalence in Japanese patients with fulminant hepatitis and chronic liver disease of unknown origin.1

To the Editor:

I permanently installed the CD-ROM into the computer hosting my training program’s World Wide Web site (operating system: Microsoft [Redmond, WA] Windows NT Server 4.0; web server: O’Reilly & Associates, Inc’s [Sebastapol, CA] WebSite Pro). I used Allaire, Inc’s (Cambridge, MA) Cold Fusion package to program an interface between WebSite Pro and the web server computer’s ODBC module. Thus, the CD-ROM effectively became accessible via any web browser (see Fig 1). Web server security was configured to limit access in compliance with the CD-ROM’s license. When displaying a Slide Bank image in the user’s browser, the interface cautions the user to give appropriate credit to the ASH Slide Bank and the original contributor of the image (as per the license).

The user surfs to the project’s home page, from which can be selected the hematologic topic of interest. Small versions (“thumbnails”) of relevant images are shown first (along with any related information, such as descriptions of the images, listed in the images’ entries in the index database); each thumbnail is linked to a larger version. Most browsers provide means for copying displayed JPEG images into other programs. Thus, it is trivial for the user to incorporate Slide Bank images into computer-based presentations that can be created with software packages such as Microsoft PowerPoint.

Recent review of web server access logs show that many hundreds of images have been accessed since the interface was made available to our faculty and trainees. Images are accessed 7 days a week at all hours of the day and night, from on- and off-campus locations. Faculty and trainees have incorporated Slide Bank images into presentations for teaching purposes. No security breaches or license violations have been identified.

This web interface to the Heme CD appears to satisfy the goals of improving access to Slide Bank images while reducing (in fact, eliminating) the risk for media damage or loss from normal use. Other hematology training programs may wish to replicate this project using their own licensed copies of the Heme CD. The interface (Cold Fusion code) is available without charge; requests can be e-mailed to afrinl@musc.edu.

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REFERENCES


Evidence Against a Direct Role Played by Transfusion-Transmitted Virus Infection in Causing Hepatic or Hematologic Manifestations

To the Editor:

Transfusion-transmitted virus (TTV) is a newly described nonenveloped, single-stranded DNA virus, recently detected with high prevalence in Japanese patients with fulminant hepatitis and chronic liver disease of unknown origin. Having a high buoyant density (1.26 g/mL) and a single-stranded DNA genome of at least 3,700 bases, TTV resembles the Parvoviridae. It could be argued that, in analogy to Parvovirus B19, which has a remarkable tropism for human erythroid progenitor cells, TTV-infected hosts may have hematologic manifestations, including anemia, leukopenia, or thrombocytopenia. However, whether TTV has any role in causing hepatic and/or hematologic diseases remains an unsettled issue. Here we report the results of searching for TTV DNA in fasting serum samples collected from 250 subjects, belonging to the following four categories: patients with chronic liver disease (N = 49), patients with coagulopathy (N = 34), intravenous drug users (N = 50), and nonremunerated blood donors (N = 117). TTV DNA sequences, determined by polymerase chain reaction (PCR), were detected in 4 of 117 (3.4%) healthy blood donors and 15 of 133 (11.3%) patients (P = .019). The prevalence of TTV DNA seropositivity was similar in the three groups of patients, being 4 of 34 (11.8%) in patients with coagulopathy, 5 of 50 (10.0%) in intravenous drug users, and 6 of 49 (12.2%) in patients with chronic liver disease (P = .935). There were no significant differences between TTV DNA+ and TTV DNA− subjects with regard to age (41.7 ± 17.8 vs 39.1 ± 14.1 years, mean ± SD; P = .535) and gender distribution (male/female ratio 13/6 v 78/153; P = .846).

Table 1. Association Between TTV Infection and Serologic Markers of Hepatitis Viruses in the Studied Groups

<table>
<thead>
<tr>
<th>Preceding Markers</th>
<th>HAV Ab−</th>
<th>HBc Ab−</th>
<th>HCV Ab−</th>
<th>HGV RNA−</th>
<th>Any of the Preceding Markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood donors (N = 4)</td>
<td>1/4</td>
<td>0/4</td>
<td>0/4</td>
<td>1/4</td>
<td>2/4</td>
</tr>
<tr>
<td>Patients with coagulopathy (N = 4)</td>
<td>NT</td>
<td>2/4</td>
<td>4/4</td>
<td>0/4</td>
<td>4/4</td>
</tr>
<tr>
<td>Intravenous drug users (N = 5)</td>
<td>NT</td>
<td>1/5</td>
<td>3/5</td>
<td>2/5</td>
<td>4/5</td>
</tr>
<tr>
<td>Chronic liver disease (N = 6)</td>
<td>4/6</td>
<td>1/6</td>
<td>5/6</td>
<td>1/6</td>
<td>6/6</td>
</tr>
</tbody>
</table>

Abbreviations: HBcAb, anti–hepatitis B core antibody; HCVAb, anti–hepatitis C virus antibody; HGV, hepatitis G virus; NT, not tested.
To the Editor:

We write to report the development of peripheral T-cell lymphoma following therapy for B-cell lymphoma with the monoclonal antibody anti-CD20 (Rituximab) in the trial recently published in Blood.1 The patient was a 59-year-old man of Anglo-Asian extraction who presented in 1992 with generalized lymphadenopathy and constitutional B symptoms. Excision biopsy yielded a diagnosis of high-grade B-cell lymphoma, polymorphic centroblastic type (Kiels), diffuse large B-cell lymphoma (ILSG), the immune phenotype being CD20+, CD79a+, Ig HCV, an agent routinely tested for by blood banks. Finally, none of the TTV-infected subjects had anemia, leukopenia, or thrombocytopenia.

The risk for viral transmission by transfusion has been reduced dramatically through improved techniques for selecting and testing blood donors.2 Initiatives to further improve the safety of the blood supply, including more stringent donor qualifications, additional testing for infectious disease markers, viral inactivation processes, and refinement of transfusion decisions are possible. However, because the risk for viral transmission by allogeneic transfusion is already low, additional measures will have a predictably limited yield and poor cost-effectiveness.3 Although efforts to improve the safety of blood supply will continue, to minimize the risks of transmitting by blood transfusion the next (yet undiscovered) agent, we will have no other choice than a judicious use of blood and blood components.

ACKNOWLEDGMENT

The authors are grateful to Dario Liani and Tiziana Galai for excellent technical support.

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REFERENCES


# Table 2. Association Between TTV Infection and Abnormal ALT in the Studied Groups

<table>
<thead>
<tr>
<th></th>
<th>TTV DNA+</th>
<th>TTV DNA-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood donors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT normal</td>
<td>11/201</td>
<td>7/143</td>
</tr>
<tr>
<td>ALT abnormal</td>
<td>8/49</td>
<td>0/5</td>
</tr>
<tr>
<td>Patients with coagulopathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT normal</td>
<td>2/25</td>
<td>0/4</td>
</tr>
<tr>
<td>ALT abnormal</td>
<td>2/9</td>
<td>0/0</td>
</tr>
<tr>
<td>Intravenous drug users</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT normal</td>
<td>4/38</td>
<td>2/12</td>
</tr>
<tr>
<td>ALT abnormal</td>
<td>1/12</td>
<td>0/0</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT normal</td>
<td>1/24</td>
<td>1/13</td>
</tr>
<tr>
<td>ALT abnormal</td>
<td>5/25</td>
<td>0/2</td>
</tr>
</tbody>
</table>

Abnormal: >1.5 the upper limit of reference range.

The rate of positivity for serum markers of infection by known or presumed hepatotropic viruses in TTV DNA positive subjects is presented in Table 1. Serum markers for hepatotropic viruses were present in 16 of 19 TTV DNA+ patients. Twelve of 19 TTV DNA+ subjects were anti-HCV antibody+, in comparison with 90 of 231 TTV DNA+ (P = .039). In nonremunerated, regular blood donors, which are selected for being at low risk for infections by parenterally transmitted viruses, TTV DNA was found in one HGV RNA positive subject and in one subject with evidence of previous exposure to HAV.

Table 2 shows the relationship between TTV DNA seropositivity and abnormal serum alanine aminotransferase (ALT) concentrations. Although TTV DNA+ subjects had more commonly ALT >1.5-fold the upper limit of the normal reference range than TTV DNA− patients (P = .010), none of the seven TTV DNA+ anti-HCV− subjects had abnormal ALT. Hemoglobin values, leukocyte count, and platelet count were similar in TTV DNA+ and TTV DNA− subjects; moreover, none of TTV DNA+ subjects had hemoglobin level <110 g/L, leukocyte count <4.0 × 10^9/L, or platelet count <50 × 10^9/L.

This report confirms that TTV infection has a worldwide distribution and a surprisingly high prevalence, both in healthy volunteer blood donors and in groups traditionally considered at risk for parenterally transmitted viral infections. However, it also casts doubts that prospective screening of blood donors for TTV will ever be indicated, at least for the purpose of avoiding posttransfusion hepatitis. In fact, none of TTV-infected blood donors had alanine aminotransferases above normal limits. Moreover, although among subjects belonging to groups at risk the presence of TTV DNA is accompanied by abnormal alanine aminotransferase in approximately 40% of cases, this might be entirely due to the frequent coexistence, in these populations, of infection by TTV-infected blood donors.5 Initiatives to further improve the safety of the blood supply, including more stringent donor qualifications, additional testing for infectious disease markers, viral inactivation processes, and refinement of transfusion decisions are possible. However, because the risk for viral transmission by allogeneic transfusion is already low, additional measures will have a predictably limited yield and poor cost-effectiveness.6 Although efforts to improve the safety of blood supply will continue, to minimize the risks of transmitting by blood transfusion the next (yet undiscovered) agent, we will have no other choice than a judicious use of blood and blood components.

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Peripheral T-Cell Lymphoma Following Rituximab Therapy for B-Cell Lymphoma

To the Editor:

We write to report the development of peripheral T-cell lymphoma following therapy for B-cell lymphoma with the monoclonal antibody anti-CD20 (Rituximab) in the trial recently published in Blood.1 The patient was a 59-year-old man of Anglo-Asian extraction who presented in 1992 with generalized lymphadenopathy and constitutional B symptoms. Excision biopsy yielded a diagnosis of high-grade B-cell lymphoma, polymorphic centroblastic type (Kiels), diffuse large B-cell lymphoma (ILSG), the immune phenotype being CD20+, CD79a+, Ig
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