the current understanding of norovirus-host interaction. In addition, several points should perhaps be reconsidered with respect to data analysis and interpretation of the results.

The ability of noroviral virus-like particles to recognize human HBGAs is highly strain-specific [2, 3], and this fact is the basis of current exploration of norovirus host range. Different HBGA binding patterns have been found in both GI and GII noroviruses [4]. Recent data even suggest variations in HBGA recognition within the GII-4 genotype [5]. Thus, it is critical for an outbreak study to have a single norovirus strain involved in each outbreak. Unfortunately, this does not appear to be the case for the study described in the Halperin et al. article [1]. The 2003 outbreak was caused by at least 2 strains that phylogenetically clustered with 2002B and 2003A of GII-4 [1], respectively. This could result in a misleading outcome if the 2 strains have different HBGA binding patterns. Similarly, data for 2 outbreaks that occurred in 2 different years and were caused by genetically distinct strains should not be pooled for analysis.

Other concerns about this study include the following. First, the low reverse transcriptase polymerase chain reaction detection rates of norovirus in the 2 outbreaks (33% and 28%, respectively) [1] raises the possibility that additional causes, such as other noroviruses and/or non-norovirus pathogens, were involved, which could further dilute the results. Second, it is known that in addition to the ABO family, the Lewis and secretor families are also involved in norovirus-host interaction. The Halperin et al. study [1] focused only on the ABO family, and another reason for the negative results could be that the important information of the secretor family was missed, as shown by several previous studies [6–8]. Third, GII is composed of at least 17 genotypes and many of them have not yet been studied in terms of virus-host interaction. Therefore, the conclusion that there is no association between HBGA and susceptibility to clinical infection with GII norovirus—based on only 2 GII-4 outbreaks—is overstated. Fourth, it would be informative if the HBGA binding patterns of the causative strains involved in the outbreaks could be determined, which would address the key question about the strain-specific host range.

Our group performed a similar study recently on 2 norovirus-associated gastroenteritis outbreaks caused by a GII-3 and GII-4 virus, respectively [9]. A significant association was observed between symptomatic infection and host secretor status. In addition, in the GII-4–caused outbreak, we found a significantly increased infection rate for type-A individuals and a decreased risk of infection for type-O individuals [9]. These results are similar to those reported in other studies [6–8], in which an association between norovirus infection and host secretor status could be readily established, whereas a correlation of ABO types with infection was variable. Thus the H epitope, the 1,2 α-fucosyltransferase (TUT2), must play the central role in the host range of those noroviruses.

Our understanding of the interaction between the polymorphic human HBGAs and the broadly diverse human noroviruses remains preliminary. Recent studies also suggested that host factor(s) may be strongly associated with the evolution and epidemiology of GII-4 noroviruses, in which both host immunity and HBGAs could play an important role [5]. Because human noroviruses remain difficult to cultivate and an effective animal model is still lacking, population studies that use epidemiological approaches remain an important tool for norovirus research.

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References


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Intitial Descriptive and Analytical Data on an Outbreak of Norovirus Infection at Marine Corps Recruit Depot Parris Island, South Carolina

To the Editor—We read with interest the brief report by Halperin et al. in which the authors found no association between histo–blood group antigens (HBGAs) and susceptibility to clinical genogroup II
Table 1. Association between histo–blood group antigen (HBGA) and susceptibility to symptomatic genogroup II norovirus infection.

<table>
<thead>
<tr>
<th>HBGA type</th>
<th>Case patients, no. (%)</th>
<th>Control patients, no. (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>25 (47)</td>
<td>26 (43)</td>
<td>1.16 (0.53–2.51)</td>
</tr>
<tr>
<td>AB</td>
<td>1 (2)</td>
<td>2 (3)</td>
<td>0.91 (0.18–4.45)</td>
</tr>
<tr>
<td>B</td>
<td>3 (6)</td>
<td>4 (6)</td>
<td>0.60 (0.06–7.08)</td>
</tr>
<tr>
<td>O</td>
<td>24 (45)</td>
<td>29 (48)</td>
<td>1.00 (reference)</td>
</tr>
</tbody>
</table>

NOTE: CI, confidence interval; OR, odds ratio.

norovirus (NoV) infection [1]. We report similar results for an outbreak of NoV infection that occurred in a United States military training facility. In 2007, an outbreak of genogroup II NoV infection was confirmed by reverse-transcriptase polymerase chain reaction (PCR) of stool samples from clinically infected recruits at the Marine Corps Recruit Depot (MCRD) Parris Island, South Carolina. A case-control study to evaluate the risk factors for symptomatic infection was approved by the institutional review board at the Naval Medical Center, Portsmouth, Virginia. Case patients were defined as those who reported gastrointestinal illness in a questionnaire. ABO blood type was abstracted from electronic medical records. Clinical characteristics of infection were collected from the electronic medical records and the questionnaire.

One hundred eighteen recruits completed risk-factor questionnaires. Four subjects were excluded because of incomplete answers. The percentages of blood types A, B, AB, and O in the study population were 45%, 6%, 3%, and 46%, respectively. Of the 114 case patients, 77% reported diarrhea, 27% reported fever, and 69% reported nausea and vomiting. The modes for the length of illness and the number of training days missed were 2 days and 1 day, respectively. Eighty-three percent of case patients missed an average of one day of training. When patients in the A, B, and AB blood groups were compared with patients in the O blood group, there was no association between HBGA and susceptibility to clinical infection with genogroup II NoV (table 1).

We provide data that further support the assertion of Halperin et al. [1] that genogroup II NoV is capable of infecting persons regardless of their ABO blood type. Furthermore, we highlight the fact that outbreaks occur frequently and are significantly costly to the military, with regard to both decreased productivity and military readiness.

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Reference

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The views expressed in this article are those of the author(s) and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

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Reply to Chan et al., Tan and Jiang, and St. Clair and Patel

To the Editor—Chan et al. speculate that the associations between gastrointestinal disease due to norovirus genogroup II genotype 4 (GII.4) and ABO histo–blood group may differ in the 2 outbreaks analyzed in our recently published article [1] as a result of changes in patterns of virus binding to histo–blood group antigens (HBGAs). In the original article, we included the outbreak as a variable in the final model to control for possible confounding. Surprisingly, an interaction term between outbreak and blood group was found not to be statistically significant, and therefore, was dropped from the final model. This analysis was performed in accordance with the knowledge at the time, which assumed no significant differences in the HBGA binding patterns of the GII.4 noroviruses involved in the 2 outbreaks. In accordance with the request made by Chan et al., we have performed a separate analysis for each of the 2 outbreaks. Indeed, when analyzing the association of clinical disease with ABO histo–blood group, a statistically significant decrease in risk was observed for the A and AB groups in the second outbreak (which took place in 2005), whereas no association was observed in outbreak 1 (which occurred during 2003) (table 1). No significant changes were demonstrated for our analysis of the association of ABO histo–blood group and fever (data not shown).

Tan and Jiang raise several issues regarding the data analysis and interpretation in our article [1]. They suggest the possibility that 2003 outbreak was caused by at least 2 strains phylogenetically clustered with 2002B and 2003A of the GII.4 strains. Bootstrap values do not support separation of the 2 strains involved in the 2003 Israeli outbreak. Furthermore, the abrupt onset and termination of the outbreak support the hypothesis that it was caused by exposure to a single common source and, therefore, to a single genotype [2]. Our previous surveillance data do not