The incidence and time course of the immune response to Vero toxin–producing *Escherichia coli* (VTEC) other than O157 (O26, O55, O111, O128) were determined in 107 children with enteropathic hemolytic uremic syndrome (HUS) by ELISA and compared to antibody profiles of 125 healthy pediatric controls and 100 children with community-acquired uncomplicated diarrhea. Six of 8 HUS patients with non-O157 VTEC isolates exhibited a serologic response to the homologous lipopolysaccharide antigen similar to that of patients infected with *E. coli* O157. In addition, elevated IgM or IgG antibodies were demonstrated in 7 of 19 culture- and O157 serology–negative HUS patients. Serogroup-specific antibodies decreased below cutoff levels within several months after convalescence. Anti–non-O157 antibodies were found in 14% of the diarrheic controls. Unexpectedly, a high proportion (27/82) of anti–O157 lipopolysaccharide antibody–positive HUS samples reacted with LPS from *E. coli* O55:B5, suggesting shared epitopes with endemic VTEC O157 strains.
Table 1. Demographic and clinical data of HUS patients and control subjects.

<table>
<thead>
<tr>
<th>Group (n)</th>
<th>Clinical diagnosis</th>
<th>Age, years, range (median)</th>
<th>VTEC isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (125)</td>
<td>Healthy</td>
<td>0.04–23 (7.2)</td>
<td>No stool cultures</td>
</tr>
<tr>
<td>2 (8)</td>
<td>E+ HUS</td>
<td>0.9–22 (1.6)</td>
<td>Non-O157*</td>
</tr>
<tr>
<td>3 (99)</td>
<td>E+ HUS</td>
<td>0.3–14.9 (2.9)</td>
<td>None</td>
</tr>
<tr>
<td>4 (100)</td>
<td>Diarrhea</td>
<td>0.06–17 (2.1)</td>
<td>Not examined for VTEC</td>
</tr>
</tbody>
</table>

NOTE. E+ HUS, enteropathic HUS; VTEC, Vero toxin–producing E. coli. Sera were from various parts of Germany (with few patient samples from Switzerland, Austria, and France [Alsace]). Group 1, ambulatory patients or children for elective surgery who had no history of HUS or recent diarrhea; group 4, community-acquired acute diarrhea without contact to HUS patients or proven VTEC infection. Stool specimens (no. positive in parentheses) were routinely screened for Salmonella (33), Shigella (2), Yersinia (1), and Campylobacter (1) species, and in infants, rotavirus (18) and adenovirus (2) and traditional enteropathogenic E. coli (4).

* VTEC O26:H1 (patients 1 and 3), O26:H1 (patient 2), O55:H6 (patient 4), O55:H11 (patient 5), O111:H5 (patient 6), and O111:H11 (patients 7 and 8); all isolates produced type 2 Vero toxin in vitro only.

ties in a large pediatric population of healthy subjects, we analyzed the magnitude, immunoglobulin class, and kinetics of the antibody response and compared it with the immune response to E. coli O157, using sera of children with HUS and with uncomplicated diarrhea.

Materials and Methods

Patient sera. Pertinent clinical, microbiologic, and demographic data are listed in table 1. Briefly, sera from 8 patients with classical (E+) HUS that was associated with fecal VTEC isolates belonging to serogroups other than O157 were examined (group 2). These patients (10 months to 22 years old; median, 1.6 years) were from Germany (n = 6) and Switzerland (n = 2). They were identified between 1983 and 1994 and were not linked epidemiologically. In addition, serum samples of 99 E+ HUS patients with negative stool cultures for VTEC, diagnosed between 1985 and 1993, were investigated (group 3).

Control sera. Samples were obtained from 125 well children of all pediatric age groups who had no history of HUS or recent diarrhea (group 1) and from 100 children with uncomplicated, acute diarrhea who had not been in contact with HUS patients (group 4). The majority of the control sera were obtained during the summer and fall to reflect the seasonal variation of the E+ HUS. All controls and most of the HUS patients were from Germany. A pooled human plasma preparation containing physiologic concentrations of the major immunoglobulin classes (Bisoko; Biotest Pharma, Dreieich, Germany) and an intravenous IgA- and IgM-enriched immunoglobulin preparation (Pentaglobin; Biotest Pharma) were used as additional controls. All serum samples were aliquoted and stored at −20°C until use.

Stool samples. Stools from HUS patients were examined for VTEC and other common enteropathogenic bacteria within the first 1 or 2 weeks after onset of HUS as described [28, 35]. Studies included slide agglutination of at least 5 lactose-fermenting colonies with E. coli O157, and typing sera for the traditional enteropathogenic E. coli (EPEC) O antigens [36], growth on sorbitol-MacConkey agar, and cytotoxicity assays. E. coli isolates were characterized biochemically and serologically, and their Vero toxin profile was determined. Stool samples of the diarrheic controls obtained on admission to hospital were routinely screened for Salmonella, Shigella, and Campylobacter species and Yersinia enterocolitica and in some instances for gastrointestinal viruses. In addition, 65 samples were also screened for traditional EPEC strains as described above but only occasionally for Vero toxin–producing E. coli (microbiologic results of group 2 and group 4 patients are summarized in the footnote to table 1).

Rabbit immune sera. Rabbit immune sera (monovalent standard agglutination sera) against the EPEC serogroups O26 (anti-O26:K60), O55 (anti-O55:K59), O111 (anti-O111:K58), and O128 (anti-O128:K67) and the pooled OK-B group antigens (pool A) were from Behringwerke (Marburg, Germany). A polyclonal anti–E. coli O157 antibody was a gift from K. Karl (Institute of Hygiene and Medical Microbiology, Würzburg, Germany).

LPS preparation. LPS from E. coli O26:B6 and O128:B12 were from Sigma (St. Louis). LPS from E. coli O55:B5 and O111:B4 were from Paesel & Lorey (Frankfurt, Germany). The E. coli O157:H− strain 493-1, originally isolated from a patient with HUS, was grown in yeast extract medium, and the LPS was extracted as described [22, 37]. All LPS preparations were separated by SDS-PAGE and visualized by silver staining [38] and immunoblotting [39], confirming the smoothness and serogroup specificity of the LPS used for the ELISA. No protein contamination was detected after staining with Coomassie blue.

SDS-PAGE and immunoblotting. LPS (6 μg/lane) was analyzed by electrophoresis in 11% (wt/vol) polyacrylamide gels using a minigel apparatus (Mini-Protean II electrophoresis cell; BioRad Laboratories, Richmond, CA). Replicate gels were fixed and stained with Coomassie blue. LPS (6 μg/lane) was analyzed by electrophoresis and stained with Coomassie blue. LPS (6 μg/lane) was analyzed by electrophoresis and stained with Coomassie blue.
IgA

1000

10000

Patient 1

Patient 2

Patient 3

Blood donor

Biseko®

IgM

Serum dilution
(reciprocals)

ELISA units

IgG

Results

Specificity and sensitivity of LPS ELISAs. Rabbit immune sera demonstrated high IgG antibody levels against homologous LPS, while the pool A serum reacted with all non-O157 LPS. No appreciable cross-reactions were observed with heterologous LPS from selected EPEC O groups or with LPS from the E. coli O157:H7 isolate. Using human sera, titration curves were established with all ELISAs. Patient sera were clearly separated from control samples over the entire range of dilutions. The resolution was highest in the range of 1/1400 to 1/2000. For the IgA and IgM ELISAs, acute patient sera revealed ~20- to 50-fold greater titers than the controls (figure 1).

Distribution of non-O157 VTEC LPS ELISA reactivities in the control population (group 1). Control sera obtained from children without a history of recent gastrointestinal illness were investigated by ELISA for their reactivity with LPS from four EPEC serogroups using heavy chain-specific conjugate antibodies against human IgA, IgM, and IgG. IgM and IgG reactivities to E. coli O26, O55, O111, and O128 LPS are shown in

Statistical analysis. Data were processed using Excel 5.0 (Microsoft, Redmond, WA) and Cricket Graph 1.3 (Cricket Software, Malvern, PA). Data were expressed as arithmetic mean values of OD readings (ELISA units) or as multiples of SDs above the mean. For statistical analysis and assessment of the means, t tests with appropriate corrections were used [40]. The level of significance was set at P < .05.

Figure 1. Titration of control sera (single blood donor and commercial plasma preparation [Biseko; Biotest Pharma, Dreieich, Germany]) and sera of 3 patients with acute enteropathic HUS associated with Vero toxin-producing E. coli O26 isolates by IgA, IgM, and IgG ELISA using homologous (O26) lipopolysaccharide antigen.
Figure 2. IgM and IgG ELISA reactivities of 125 sera of well pediatric controls plotted against age of donor. Horizontal dotted lines represent break points calculated for each assay (arithmetic means +3 SD). Break points for IgA ELISAs were as follows: for O26, 16 ($r^2 = .008$); for O55, 24 ($r^2 = .025$); for O111, 16 ($r^2 = .010$); for O128, 28 ($r^2 = .102$). LPS, lipopolysaccharide.
Table 2. Antibodies to lipopolysaccharide (LPS) antigens in HUS associated with non-O157 Verotoxin-producing E. coli (VTEC) (group 2).

<table>
<thead>
<tr>
<th>Isolate</th>
<th>O26</th>
<th>O55</th>
<th>O111</th>
<th>O128</th>
<th>O157</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTEC O26 (n = 3)</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>VTEC O55 (n = 2)</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>VTEC O111 (n = 3)</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total (n = 8)</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

NOTE: IgM and/or IgG ELISA results above cutoff level were considered positive. Homologous reactions are in bold. Relative antibody levels are shown in figure 2.

* Serum of patient 3 reacted with all 5 LPS antigens.
† Serum of patient 7 reacted with O26 and O111 LPS antigens.

figure 2. We observed a slight trend towards greater ELISA units with increasing age of the donor; however, the differences of the arithmetic means of the OD values between the younger and older children (cutoff, 10 years) did not reach significance (P > .05 for all assays). The highest ELISA reactivities in the control group were demonstrated with the O111 LPS IgG assay. Mean IgG ELISA values for various LPS antigens differed significantly (P < .01). In contrast, no significant differences were found for IgA and IgM (P > .05 for all assays). The break points derived from these controls were applied to the analysis of patient sera. Eight controls had IgM and/or IgG antibodies above the respective cutoffs. Four of them reacted with more than one LPS antigen. Their antibody levels were generally only slightly above the break point (see figure 2).

LPS-specific antibodies in HUS patients with non-O157 VTEC isolates (group 2). Acute serum samples of 8 HUS patients with VTEC isolates other than serogroup O157, namely O26, O55, and O111, were examined for the presence of antibodies against LPS derived from homologous and heterologous E. coli serogroups. The level of antibodies detected by ELISA varied among patients and associated VTEC serogroups: All 5 patients with VTEC O26 or O55 isolates had elevated IgA, IgM, and IgG antibodies (acute and/or convalescent sera) against the homologous LPS. In contrast, 2 of 3 patients with VTEC O111 isolates lacked a detectable immune response, while only low-titer antibodies of the IgM (and IgA) class were detected in the third patient (table 2). In comparison, 19 of 20 HUS patients with E. coli O157:H7 or O157:H− isolates exhibited diagnostic anti-O157 LPS antibodies (unpublished data). ELISA results were in complete agreement with immunoblot results; that is, all ELISA-positive sera were positive by immunoblot, while the 2 ELISA-negative sera from patients with VTEC O111 isolates were also negative by immunoblot (results not shown).

To determine the serogroup specificity of the LPS ELISAs and their diagnostic validity using patient sera, samples of all 8 group 2 patients were tested with a panel of heterologous LPS antigens, including O157 LPS. The serum of a patient with a VTEC O26:H− isolate (patient 3) reacted with multiple LPS antigens; the serum of a patient with a VTEC O111 isolate (patient 7) showed weak positive reactions in the O111 and the O26 LPS ELISA (both IgM). None of the remaining sera reacted with heterologous LPS (table 2). A synopsis of the immune responses is shown in figure 3. For easier comparison, ELISA results were expressed as multiples of the SDs (SD units) above the mean of the pediatric control sera. Note that bars are invisible because of scale at low ELISA reactivities (< 1SD above the mean of healthy controls); that is, no bars indicate negative results.

HUS patients without VTEC isolate (group 3). Serum samples from 99 HUS patients from whom VTEC isolates had not been recovered were examined for antibodies of all three immunoglobulin classes to O26, O55, O111, O128, and O157 LPS by ELISA. Eighty-five of the 99 patients had IgA, IgM, or IgG antibodies above the cutoff level. Three of the 85 samples reacted only in IgA ELISAs. Mean and range of anti-O157 LPS antibody levels of the remaining 82 samples were similar to those of patients with microbiologically proven VTEC O157 infection (data not shown).

Of the 17 HUS patients lacking IgM and/or IgG antibodies to O157 LPS, 8 reacted with one or more of the non-O157 antigens tested. A single sample was positive only in the IgA ELISA (O111 LPS), while the remaining 7 patients exhibited IgM and/or IgG antibodies against non-O157 antigens (41% of the anti-O157 antibody–negative patients): O26, 3 patients; O55, O111, O128, O26, and O55, 1 each (table 3). The acute-phase serum was diagnostic in 6 of these patients, and the other became positive during convalescence (anti-O26 and –O55 LPS IgG, patient 11). The magnitude of the immune response of the 7 non–O157 LPS antibody–positive patients is shown in figure 4. Based on our observation that IgA ELISA results were occasionally positive (i.e., above the cutoff level) without detectable homologous IgM or IgG antibodies, sole IgA reactivities were not considered diagnostic. Data are summarized in table 4.

The sera of 45 of 82 HUS patients with an established IgM and/or IgG immune response to O157 LPS reacted also with
non-O157 LPS antigens. In 12 of the 45 samples, the reactions with non-O157 LPS antigens were confined to IgA ELISAs and were largely restricted to the O55 LPS antigen (10/12 cases). Antibody reactivities of the remaining 33 patients against the panel of LPS antigens are shown in table 4. The majority of the sera that showed an immune response to non-O157 LPS in addition to O157 LPS reacted with LPS derived from *E. coli* O55:B5 (27/33; tables 3 and 4). In contrast, the
frequency of antibodies to 055 LPS was low in HUS patients with microbiologically confirmed non-0157 E. coli infection (group 2), which is in keeping with the frequency of VTEC 055 isolates in this group (table 2, figure 3). Moreover, one-third of HUS patients with 0157 isolates also had antibodies to 055 LPS (unpublished data), indicating shared epitopes between EPEC 055:B5 and endemic VTEC 0157 strains.

To explore the potential importance of antibodies to non-0157 VTEC serovars, especially in patients with multiple reactivities, antibody levels to non-0157 antigens were directly plotted against antibody levels to 0157 LPS. Examples are shown in figure 5. No correlation was observed between anti-026 and anti-0157 reactivities. This indicates that high antibody levels to 026 LPS, and similarly to 0111 and 0128 LPS (data not shown), result from specific immunologic stimulation. In contrast, increased 055 LPS ELISA reactivities corresponded to elevated 0157 LPS antibody levels, suggestive of cross-reactivity (figure 5).

Control patients with uncomplicated diarrhea (group 4). Sera of 100 children with acute diarrhea who had no contact with HUS patients or cases of proven or suspected VTEC infection were examined to assess the incidence of non-0157 LPS antibodies in patients with uncomplicated gastrointestinal illnesses. Fourteen percent tested positive for one (n = 10) or more (n = 4) E. coli serogroups as defined by the detection of elevated IgM and/or IgG antibodies (026 > 055 = 0128 > 0111). The sera of 3 additional patients reacted only in the IgA ELISA. Two patients had low-level IgG antibodies against the 0157 LPS. Traditional EPEC strains were isolated from 4 children, namely serogroups 026, 0119 from 2, and 0125. The infant with EPEC 026 diarrhea revealed a strong serogroup-specific immune response pertinent to all three immunoglobulin classes, while sera of the remainder did not react with any of the heterologous LPS antigens tested.

Kinetics of anti-LPS antibodies. During convalescence, a rapid decline in IgA and IgM antibodies to non-0157 LPS was documented in most patients with appropriate follow-up samples. A transient rise of IgG antibodies was observed in 3 of 6 patients during the acute or postacute phase. The few cases with late samples revealed a decrease in anti-LPS
Table 4. Distribution of ELISA reactivities to heterologous lipopolysaccharide (LPS) antigens in sera from children with HUS.

<table>
<thead>
<tr>
<th>Result category (range of SD units)</th>
<th>O26 (n = 31)</th>
<th>O55 (n = 32)</th>
<th>O111 (n = 32)</th>
<th>O128 (n = 32)</th>
<th>O157 (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgA</td>
<td>27</td>
<td>12</td>
<td>24</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>IgM</td>
<td>28</td>
<td>12</td>
<td>30</td>
<td>31</td>
<td>2</td>
</tr>
<tr>
<td>IgG</td>
<td>28</td>
<td>6</td>
<td>31</td>
<td>31</td>
<td>4</td>
</tr>
<tr>
<td>IgG</td>
<td>18</td>
<td>6</td>
<td>28</td>
<td>24</td>
<td>31</td>
</tr>
<tr>
<td>IgA</td>
<td>31</td>
<td></td>
<td>28</td>
<td>31</td>
<td>2</td>
</tr>
<tr>
<td>IgM</td>
<td>30</td>
<td></td>
<td>24</td>
<td>23</td>
<td>7</td>
</tr>
<tr>
<td>IgG</td>
<td></td>
<td>10</td>
<td>10</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. Sera from 82 HUS patients without Vero toxin–producing E. coli isolates had serologic evidence of E. coli O157 infection (elevated IgM and/or IgG anti–O157 LPS antibodies by ELISA). Sera from 33 reacted with 1 of 4 non–O157 LPS antigens.

* Some samples were positive in >1 ELISA.

† Results are given as fold SDs above mean of healthy pediatric control group. Break points were set at 3SD above mean for each LPS antigen and immunoglobulin class.

IgG antibodies below the cutoff level within several months (figure 6).

Discussion

In the present study, we systematically analyzed the humoral immune response of pediatric HUS patients to a panel of non-O157 VTEC serogroups by ELISA. In addition, the incidence of antibodies to the same antigens was examined in children with uncomplicated diarrhea. Since the prevalence of antibodies to E. coli O26, O55, O111, and O128 in our population was not known, we also screened control sera of all pediatric age groups. Results derived from the control population suggest the presence of IgG antibodies to O111 LPS with a trend toward increasing levels with age. IgG levels to the remaining O antigens, including O157, were considerably lower, while no LPS type–related differences were observed with the IgM ELISAs. This may reflect varied past exposures to homologous or cross-reactive bacterial epitopes associated with a lasting IgG response to some LPS antigens in the population studied. Of interest, using an indirect hemagglutination technique, Neter et al. [41] reported 40 years ago that healthy individuals had higher antibody titers with increasing age against common EPEC O antigens.

Few studies have addressed the frequency of non-O157 VTEC isolates from HUS patients [15, 22, 42, 43] or from patients with VTEC-associated diarrhea [5, 7, 12, 44–46]. In our continuing study of the role of Vero toxin–producing E. coli in pediatric HUS in Germany, overall slightly <10% of the HUS patients had evidence by bacterial isolation and/or LPS serology of non-O157 VTEC infection, with O26 being the most common serogroup (unpublished data). Serologic results presented in this study accord with the incidence of the implicated non-O157 VTEC serovars.

Our data indicate that patients with HUS associated with infection by non-O157 VTEC strains can develop a robust, O group–specific immune response similar to patients with E. coli O157:H7 infection. We detected homologous antibodies in sera of 6 of 8 HUS patients with non-O157 VTEC isolates. Subsequently, 7 of 17 VTEC culture– and O157 LPS antibody–negative patients were found to possess elevated antibodies to non-O157 LPS. In the absence of an immune response to O157 LPS, detection of high antibody levels to non-O157 LPS strongly suggests recent infection by corresponding E. coli serovars. Thus, a probable serologic diagnosis was possible in 41% of formerly undiagnosed patients using this panel of LPS ELISAs.

However, we failed to detect an appropriate antibody response in 2 of the 3 patients with fecal VTEC O111 isolates. In contrast, serum from another patient with a Vero toxin–producing O26:H11 isolate reacted strongly with O26 and O157 LPS and, to a lesser extent, with O55, O111, and O128 LPS (patient 3, figure 3). These examples raise the possibility that a Vero toxin–producing strain, isolated during acute HUS, may not be the disease-causing agent. Indeed, isolation of differing VTEC serovars from the same patient, including E. coli O157, has been reported [7, 45, 47]. While E. coli O26:H11, O26:H1, and other non-O157 VTEC strains have clearly been implicated in the pathogenesis of HUS [1, 2], their relative role in the individual patient concomitantly infected with E. coli O157 is difficult to assess.

This study confirms earlier results demonstrating that the majority of E. coli HUS patients have elevated or rising antibody levels to E. coli O157 LPS [21, 24, 25, 27, 28]. However, more than one-third of the sera reacted with additional LPS antigens (see table 3). The vast majority of these samples had antibodies to O55 LPS derived from EPEC O55:B5 in addition to antibodies to O157. E. coli O157:H7 can cause severe colonic inflammation [48, 49]. Increased mucosal permeability allows anti-
Figure 5. Correlation between antibody levels in children with enteropathic HUS to *E. coli* O157 and non-O157 lipopolysaccharide (LPS) antigens (derived from *E. coli* O26:B6 and O55:B5) as measured by ELISA. Antibody levels are expressed as multiples of SDs above mean of controls (SD units). Break points are indicated by dotted lines.

Figure 5. The correlation between antibody levels in children with enteropathic HUS to *E. coli* O157 and non-O157 lipopolysaccharide (LPS) antigens (derived from *E. coli* O26:B6 and O55:B5) as measured by ELISA. Antibody levels are expressed as multiples of SDs above mean of controls (SD units). Break points are indicated by dotted lines.

IgM

\[ r^2 = 0.149 \]

IgG

\[ r^2 = 0.025 \]

IgM

\[ r^2 = 0.525 \]

IgG

\[ r^2 = 0.404 \]

The observation that sera from patients with *E. coli* O157 infection react with the O55 LPS is interesting in view of the close genetic relationship between VTEC O157:H7 and EPEC O55:H7, an *E. coli* strain associated with worldwide outbreaks of infantile diarrhea [54]. Other *E. coli* O55 strains, particularly O55:H6 and O55:H−, are genetically much more diverse and not necessarily closely related to EPEC O55:H7 [54]. *E. coli* O157:H7 differs from *E. coli* O55:H7 by only one electromorph, that of 6-phosphogluconate dehydrogenase (6PGD; EC 1.1.1.44), which is encoded by the *gnd* locus [55]. In *E. coli*, *gnd* is adjacent to the *rfb* cluster [56], which encodes the enzymes necessary for the synthesis of the unique antigenic O side chain component of LPS. Whittam [55] suggested that the ancestral O55:H7 clone experienced a recombination event involving part or all of *gnd* and the contiguous *rfb* cluster, resulting in an organism with a different 6PGD electromorph and O antigen. Our data indicate that some epitopes remain identical between the *E. coli* O157 and *E. coli* O55 O side chains, suggesting that some sequences of the *rfb* cluster may be preserved in the two serovars.

Diarrhea from EPEC can induce an O group–specific immune response [41, 57, 58], also shown in this study (group 4). The discrepancy between the frequency of elevated anti-
LPS antibodies and the frequency of EPEC or VTEC isolates in the diarrheic control group may be explained by the fact that only about two-thirds of the stool samples were screened for these pathogens. Other confounders are the lack of sensitivity of traditional EPEC screening methods and, possibly, discontinuation of bacterial shedding at the time of specimen sampling. In addition, 50% of the serum samples were positive for IgG only, which may indicate past infection unrelated to the cause of diarrhea at the time when the serum was collected. Alternatively, cross-reactions with other enteropathogens may occur [52, 59]. Careful studies with more sensitive identification techniques are needed to reconcile these findings. The intriguing question, whether previous exposure to certain EPEC strains protects against infections by corresponding VTEC serogroups, remains to be evaluated. For example, it is possible that the low frequency of VTEC-associated HUS observed in less-developed countries or among lower socioeconomic classes [12, 14, 60–62] is the result of O group-specific or cross-reactive (mucosal) immunity acquired during infancy.

In conclusion, we provide additional evidence that non-O157 VTEC strains are associated with classical childhood HUS and that they can induce a strong antibody response against outer membrane components of the organism. Future studies are needed to firmly establish the utility of LPS-based serologic techniques for the acute and retrospective diagnosis of non-O157 VTEC infections. Elucidation of cross-reactions between O antigens from related VTEC and EPEC clones may improve the interpretation of serologic results and offer insight into the evolution of these “new” pathogens, which are increasingly recognized as causes of outbreaks of diarrhea and HUS in various parts of the world.

Acknowledgments

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References


