Preventing Household Transmission of Shiga Toxin–Producing *Escherichia coli* O157 Infection: Promptly Separating Siblings Might Be the Key

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**Background.** Preventing household transmission of Shiga toxin–producing *Escherichia coli* O157 (STEC O157) infection is important because of the ease of interpersonal transmission and the potential disease severity.

**Methods.** We conducted a retrospective cohort study of households associated with an outbreak of STEC O157 infection in South Wales, United Kingdom, in autumn 2005. We investigated whether characteristics of the primary case patient or the household were predictors for secondary household transmission of STEC O157 infection. Furthermore, we estimated the proportion of cases that might be prevented by isolation (e.g., hospitalization) of the primary case patient immediately after the microbiological diagnosis and the number of patients with STEC O157 who would need to be isolated to prevent 1 case of hemolytic uremic syndrome. Based on dates of symptom onset, case patients in households were classified as having primary, coprimary, or secondary infection. Secondary cases were considered to be preventable if the secondary case patient’s symptoms started >1 incubation period (4 days) after the date of microbiological diagnosis of the primary case.

**Results.** Eighty-nine (91%) of 98 eligible households were enrolled. Among 20 households (22%), 25 secondary cases were ascertained. Thirteen secondary cases (56%) occurred in siblings of the primary case patients; hemolytic uremic syndrome developed in 4 of these siblings. Presence of a sibling (risk ratio, 3.8; 95% confidence interval, 0.99–14.6) and young age (<5 years) of the primary case patient (risk ratio, 2.03; 95% confidence interval, 0.99–41.6) were independent predictors for households in which secondary cases occurred. Of the 15 secondary cases for which complete information was available, 7 (46%) might have been prevented. When restricting isolation to primary case patients who were aged <10 years and who had a sibling, we estimated the number of patients who would need to be isolated to prevent 1 case of hemolytic uremic syndrome to be 47 patients (95% confidence interval, 16–78 patients).

**Conclusions.** Promptly separating pediatric patients with STEC O157 infection from their young siblings should be considered.

**BACKGROUND**

On Friday 16 September 2005, the National Public Health Service for Wales was notified of the first cases of bloody diarrhea in what became the second-largest outbreak of Shiga toxin–producing *Escherichia coli* (STEC) O157 infection in the United Kingdom [1]. Eventually, there were 157 cases that met the clinical case definition, 118 of which were microbiologically confirmed. Primary cases mostly involved children who attended 44 schools (mainly elementary schools) in 4 local authorities. Thirty-one patients were hospitalized, 11 of whom developed hemolytic uremia syndrome (HUS), and tragically, one 5-year-old child died. The vehicle of infection was delicatessen meat produced by a single supplier that was served in school meals.

The National Assembly for Wales set up the *E. coli* Public Inquiry to undertake a thorough investigation into the outbreak under The Inquiries Act 2005. The Act enables a public inquiry to be held when events have caused or are capable of causing public concern or if there is public concern that particular events may...
have occurred. The Inquiry’s terms of reference are “[to] inquire into the circumstances that led to the outbreak of E. coli O157 infection in South Wales in September 2005, and into the handling of the outbreak; and to consider the implications for the future and make recommendations accordingly” [2]. The Inquiry has legal power to call witnesses and to compel witnesses to give evidence, either in writing or orally, and to produce any relevant documents.

The Outbreak Control Team had identified the vehicle of infection by Sunday 18 September. The Inquiry has stated that the Team “succeeded in identifying a common link between the cases at a very early stage. They reacted with commendable speed and applied a precautionary and very wise approach that led to early steps being taken to remove cooked meat from the food chain” [3]. However, despite the rapid removal of the primary source of infection, secondary transmission occurred. This article investigates the potential of isolating pediatric patients with STEC O157 infection to prevent secondary household transmission.

INTRODUCTION

STEC O157 infection can cause life-threatening HUS, especially in children. Secondary infection due to STEC O157, compared with secondary infection due to most other bacterial enteric pathogens, through person-to-person transmission is common [4] and well documented in various settings (e.g., child day care facilities [5, 6], nursing homes [7], and households [8]). Considering both the ease of interpersonal transmission and the potential disease severity, preventing secondary transmission of this pathogen presents a difficult but important challenge for infection control. Importantly, even for large foodborne outbreaks of STEC O157 infection, it has been estimated that a modestly effective strategy to interrupt secondary transmission could result in a reduction of 5%–11% of symptomatic cases of STEC O157 infection [9].

In most countries, including the United States, pediatric patients with STEC O157 infection are excluded from school or nursery and, unless hospitalized, usually are cared for at home. To prevent secondary household spread, persons providing care are suitably advised about appropriate enteric precautions [10], particularly the necessity for thorough and frequent hand washing with soap [11]. The effectiveness of measures, such as prompt isolation of the primary case patient (e.g., by hospitalization [12]), for preventing household transmission has not yet been investigated. Analyzing the characteristics of households where secondary transmission has occurred may allow for a more targeted infection-control policy.

In autumn 2005, a large foodborne outbreak of infection due to STEC O157:H7 (hereafter referred to as STEC O157) occurred in South Wales, United Kingdom, predominantly affecting school-aged children in 46 different schools [13]. Subtyping of isolates by PFGE suggested that all cases comprised a single outbreak group. More than 1 case occurred in several households, and secondary transmission of infection among household members was frequently suspected. The objectives of this study were 2 fold. First, we sought to investigate whether characteristics of the primary case patient or the household structure were predictors for households where secondary cases had occurred. Second, we estimated the proportion of cases that might be prevented by isolation of the primary case patient immediately after microbiological diagnosis and the number of patients who would need to be isolated (NNI) to prevent 1 case of HUS, to assess the potential effectiveness of this intervention for the prevention and control of STEC O157 infection.

MATERIAL AND METHODS

Study design and definitions. We conducted a retrospective cohort study including non–single-person households in which at least 1 outbreak case of STEC O157 infection occurred from 15 September through 1 November 2005 in the 3 most affected local authority areas in South Wales (i.e., Caerphilly, Merthyr Tydfil, and Rhonda-Cynon-Taf). Information from records on patients and their contacts, collected as part of the outbreak investigation, was collated through personal interviews with environmental health officers in December 2005.

A case patient was defined as any person residing in the study area and presenting with either a culture-confirmed STEC O157 infection or bloody diarrhea from September through October 2005 (the working definition for case patients during the outbreak investigation). A primary case patient was defined as the person with the earliest date of onset of symptoms in the household. A household was any residence where a primary case patient to prevent secondary house-
Table 1. Classification of households according to characteristics of primary case patients and occurrence of cases in household contacts in a large outbreak of Shiga toxin–producing Escherichia coli (STEC) O157 infection in South Wales, United Kingdom, 2005.

<table>
<thead>
<tr>
<th>Characteristic of the primary case patient</th>
<th>No. of primary case patients</th>
<th>No. of households in which a secondary case occurred</th>
<th>No. of households in which a secondary case did not occur</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic, culture-confirmed STEC O157 infection</td>
<td>56</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>Bloody diarrhea; no evidence of STEC O157 infection</td>
<td>28</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Asymptomatic, culture-confirmed STEC O157 infection</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>89</strong></td>
<td><strong>20</strong></td>
<td><strong>5</strong></td>
</tr>
</tbody>
</table>

Table 2. Secondary attack rates among household contacts in a large outbreak of Shiga toxin–producing Escherichia coli O157 infection in South Wales, United Kingdom, 2005, by family relation to the primary case patient.

<table>
<thead>
<tr>
<th>Relationship of the secondary case patient to the primary case patient</th>
<th>No. of secondary case patients/ no. of household contacts</th>
<th>Attack rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sibling</td>
<td>14/107</td>
<td>13</td>
</tr>
<tr>
<td>Mother</td>
<td>6/82</td>
<td>7</td>
</tr>
<tr>
<td>Grandparent</td>
<td>3/83</td>
<td>4</td>
</tr>
<tr>
<td>Other close contacts&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2/197</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>5/469</strong></td>
<td><strong>5</strong></td>
</tr>
</tbody>
</table>

NOTE. Secondary cases included asymptomatic cases that occurred in grandparents (n = 2), mothers (n = 2), and a sibling (n = 1).

<sup>a</sup> Included other family members, friends, neighbors, and other contacts.
lowed us to retrospectively assess how accurately households in which secondary cases occurred could have been identified.

We also estimated the proportion of symptomatic cases that potentially could have been prevented by isolating all primary case patients immediately after these patients received their microbiological diagnosis. This was done by calculating the proportion of secondary cases patients who experienced the onset of symptoms ≥5 days after corresponding patients received their microbiological diagnosis. We used this number as the estimate of the absolute risk reduction (ARR) among households in which secondary cases occurred, had such an intervention been applied.

To estimate the NNI to prevent 1 case of HUS, we modified the standard calculation for the “number needed to treat” measure (1/ARR) [18, 19] by multiplying the ARR by the proportion of households in which secondary cases occurred (P_{secondary cases}). This approach took into account the fact that some households where the intervention would be applied were not at risk (i.e., households in which a secondary case did not occur). We then multiplied this estimate by a factor of 10 on the basis of the assumption that the risk of patients with STEC O157 infection developing HUS, which is strongly age dependent, is estimated to be ∼10% [20–22],

$$\text{NNI} = \left( \frac{1}{\text{ARR} \times P_{\text{secondary cases}}} \right) \times 10$$

Because it is probably impractical to strictly isolate all primary case patients, we also calculated this measure for primary case patients from at-risk households only (NNI_{HH at risk}). To perform this calculation, we used the same formula but replaced the proportion of households in which secondary cases occurred with the PPV for classifying households as being at risk for having secondary cases.

$$\text{NNI}_{\text{HH at risk}} = \left( \frac{1}{\text{ARR} \times \text{PPV}} \right) \times 10$$

We calculated 95% CIs for the NNI measure, assuming that the estimated proportions were independent and following a binomial distribution, taking into account the Gaussian propagation of errors of single estimates contained in the formulas.

**RESULTS**

**Study population.** We enrolled 89 (91%) of the 98 households in which at least 1 case occurred. Households were excluded, because a nonprimary case patient attended a school that was associated with the outbreak (n = 5), the information was incomplete (n = 3), and the household was a single-person household (n = 1). At least 1 secondary case occurred in 20 households (22%) (table 1). Altogether, 469 household contacts were ascertained, 107 of whom were siblings (median number of contacts per household, 5; range, 1–19); 278 (59%) were household contacts living in the main residence of the primary case patient.

The median age of the 89 primary case patients was 7 years (range, 1–59 years), and 75% were <10 years of age. In 11 households, the primary case patient was an adult. No secondary case was observed in contacts of these households. Also, fewer contacts lived in these households, compared with households in which the primary case patient was not an adult (median number of contacts, 3 vs. 5; P = .012). Of the 89 primary case patients, 56 (63%) had both gastroenteritis and a culture-confirmed STEC O157 infection (table 1).

There were 25 secondary case patients (secondary attack rate, 5%) living in 20 households; 24 of these patients had culture-confirmed STEC O157 infection. The median difference in dates of symptom onset between case patients with primary and secondary infection was 9 days (range, 5–26 days) (figure 1). In 18 (90%) of 20 households in which a secondary case occurred, the primary case patient had symptomatic, culture-confirmed STEC O157 infection (table 1). Fourteen secondary case patients (56%) were female, and 5 were asymptomatic; the median age of these patients was 7 years (range, 1–71 years). All 25 secondary cases occurred in family members, 22 of whom lived at the same residence as the primary case patients (secondary attack rate, 8%) and 3 of whom (all adult caregivers)
lived at a different residence (secondary attack rate, 2%). Fourteen secondary case patients (56%) were siblings of the primary case patient (median age, 5 years; range, 1–8 years), and 6 were mothers (table 2). HUS developed in 4 of the 107 siblings (secondary attack rate for HUS among siblings, 3.7%; 95% CI, 1.0%–9.3%). In 18 (90%) of the households in which a secondary case occurred, a sibling of the primary case patient lived in the household (table 3).

**Risk factor analysis.** Primary case patients who stayed in households in which secondary cases occurred were significantly younger (median age, 5 years; range, 1–10 years) than such patients who stayed in households in which a secondary case did not occur (median age, 8 years; range, 2–59 years; \( P < .001 \)) (table 3). A higher number of household contacts stayed in the main residence with the primary case patient stayed in households in which secondary cases occurred than stayed in households in which a secondary case did not occur (median number of such contacts, 4 vs. 3; \( P = .02 \)). Among dichotomous risk factors, all of the households in which the primary case patient was male, was aged <5 years, had a sibling, or had symptomatic culture-confirmed STEC O157 infection had a higher risk of having a secondary case in the household (table 3).

In the final regression model, secondary cases were more likely to occur in households in which the primary case patient had a sibling (RR, 3.81) and the primary case patient was aged <5 years (RR, 2.03) (table 3). The strongest point estimate of effect was for households in which the primary case patients had symptomatic, culture-confirmed STEC O157 infections (RR, 5.0).

**Potentially preventable cases and NNI.** Complete information was available for 15 of the 25 secondary case patients (for 5 patients, there was no date of symptom onset, because they were asymptomatic, and for 5 more patients, the date when the primary case patient received the microbiological diagnosis was unknown). Seven (46%) of the 15 secondary cases were considered to be preventable. This equates to an estimated ARR of 0.5 (95% CI, 0.2–0.7) for immediate isolation of all primary case patients. Of the 89 households, 35 (39%) were retrospectively classified as at risk for having a secondary case (table 4). Among these households were 16 (80%) of the 20 households with secondary case patients, including all 4 households with secondary case patients with HUS.

The NNI to prevent 1 case of HUS was estimated to be 95 (95% CI, 38–200). If the isolation policy was restricted to primary case patients in at-risk households only, 47 (95% CI, 16–78) primary case patients aged <10 years would need to be isolated to prevent 1 case of HUS. Furthermore, isolation would be required in only 39% of all households, although 4 (20%) of the 20 households in which secondary cases occurred would be missed because they were incorrectly classified as not being at risk. These households included the only 2 in which the primary case patient did not have his or her infection microbiologically confirmed; in the other 2 households, the secondary case patients were adult caregivers of a primary case patient who lived at another residence.

**DISCUSSION**

In this cohort study, basic information about primary case patients and their households was predictive of households where secondary cases of STEC O157 infection occurred. Household transmission occurred mostly from children (aged <10 years) with culture-confirmed infection to their young siblings. Young age of the primary case patient (<5 years) and the presence of a sibling independently increased the risk of households having secondary cases. Isolation of all symptomatic primary patients immediately after they receive microbiological diagnoses of STEC O157 infection could potentially decrease the number of secondary household cases by 50%. By focusing on households where the primary case patient is aged <10 years and has a sibling, we estimated the NNI to prevent 1 case of HUS to be 47 patients (95% CI, 16–78 patients). This suggests a large preventive potential for this intervention.

Our results are in concordance with a previous study of sporadic STEC O157 infection in Wales [8], in which young age of the primary case patient (<5 years) and of the household contact conferred the greatest risk of transmitting and acquiring STEC O157 infection, respectively. Young age has also been documented as a risk factor for secondary spread in a study of household transmission of gastroenteritis, irrespective of the infectious agent [23]. The secondary attack rate in our study (5% among all household contacts and 8% among contacts living in the main household of the primary case patient) is similar to that found in the study of sporadic STEC O157 infection in Wales (4%–15%) [8] and in the study of all-cause gastroenteritis (9%) [23]. However, some caution must be exercised when comparing secondary attack rates among studies, because these rates largely depend on the definitions of cases, households, and household contacts.

Diarrheal illness in a family member is a risk factor for developing HUS [24, 25]. A Canadian study estimated that contact with a household member with diarrhea accounted for >50% of pediatric HUS study cases [24], underpinning the need for an appropriate prevention measure. To prevent the household transmission of STEC O157 and, probably, of other pathogens causing gastroenteritis, a key strategy appears to be the prompt separation of primary patients from their sibling(s) or other young household members. For instance, either the primary patient or the vulnerable sibling(s) could be temporarily cared for by relatives or friends, as suitably advised. Alternatively, primary case patients could be isolated in a hospital, although in a large outbreak, such as this one, not enough
Table 3. Risk factors for households having a secondary case patient in a large outbreak of Shiga toxin–producing Escherichia coli O157 infection in South Wales, United Kingdom, 2005.

<table>
<thead>
<tr>
<th>Risk factor (characteristic of the primary case patient)</th>
<th>Exposed household</th>
<th>Unexposed household</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of households</td>
<td>No. of households</td>
<td>Risk ratio (95% CI)</td>
</tr>
<tr>
<td></td>
<td>with secondary</td>
<td>with secondary</td>
<td>Bivariable analysis,</td>
</tr>
<tr>
<td></td>
<td>case patients/</td>
<td>case patients/</td>
<td>risk ratio (95% CI)</td>
</tr>
<tr>
<td></td>
<td>total no. of</td>
<td>total no. of</td>
<td></td>
</tr>
<tr>
<td></td>
<td>households</td>
<td>households</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Attack rate, %</td>
<td>Attack rate, %</td>
<td></td>
</tr>
<tr>
<td>Age &lt;5 years</td>
<td>9/20</td>
<td>11/69</td>
<td>2.82 (1.36–5.83)</td>
</tr>
<tr>
<td>Male sex</td>
<td>13/41</td>
<td>7/48</td>
<td>2.17 (0.95–4.93)</td>
</tr>
<tr>
<td>Had a sibling living in the same household</td>
<td>18/63</td>
<td>2/26</td>
<td>3.71 (0.93–14.88)</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>3/16</td>
<td>17/73</td>
<td>0.80 (0.7–2.42)</td>
</tr>
<tr>
<td>Developed hemolytic uremic syndrome</td>
<td>1/4</td>
<td>19/84</td>
<td>1.10 (0.19–6.32)</td>
</tr>
<tr>
<td>Symptomatic and had culture-confirmed infection</td>
<td>18/56</td>
<td>2/33</td>
<td>5.30 (1.31–21.42)</td>
</tr>
</tbody>
</table>

Table 4. Positive predictive value (PPV) and sensitivity for classifying households as at risk for secondary transmission in a large outbreak of Shiga toxin–producing Escherichia coli O157 infection in South Wales, United Kingdom, 2005, based on variables retained in a multivariable risk factor model.

<table>
<thead>
<tr>
<th>Age of the primary case patient, years</th>
<th>At-risk household</th>
<th>Household not at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In which a secondary case occurred</td>
<td>In which a secondary case did not occur</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>&lt;5</td>
<td>16</td>
<td>4</td>
</tr>
</tbody>
</table>

NOTE. At-risk households were defined as households where the primary case patient with the culture-confirmed infection had symptoms and a sibling. PPV was defined as the proportion of at-risk households in which secondary cases occurred. Sensitivity was defined as the proportion of households in which secondary cases occurred that were correctly classified as being at risk.
have a culture-confirmed infection. It is possible that some of these primary case patients were misclassified and did not actually have STEC O157 infection. Alternatively, there may have been few organisms present in stool specimens from these patients. Thus, infection may have gone unrecognized by the conventional culture-based detection methods used in this outbreak, which are less sensitive than those based on detecting Shiga toxin genes by PCR [27]. It would also be a plausible explanation for why the risk for secondary spread was lower in these households.

This study has a number of limitations, mainly related to some of the underlying assumptions. For example, we assumed that household transmission always resulted from person-to-person transmission, although there is evidence that household transmission may also occur through contaminated objects (e.g., through towel sharing [28]). Therefore, isolation of pediatric patients with STEC O157 infection should always be accompanied by other enteric precautions in the household, such as separate washing of bed linens, towels, and soiled clothing and appropriate cleaning of toilet seats and flush handles [11]. Furthermore, a few secondary case patients may have acquired infection outside the household (e.g., in school). The assumption that the incubation period for all cases was 4 days, although in line with published data on incubation periods, may have led to some misclassification of household contact cases. When performing sensitivity analysis on the data set, assuming incubation periods of 3 days and 7 days, we obtained a similar strength of association for the identified risk factors (data not shown). Finally, we were not able to obtain more-detailed exposure information about households that might have allowed us to more precisely characterize the circumstances in which secondary transmission had occurred. However, clinicians in general practice are already flooded with guidelines [29], and therefore, it is debatable whether using a more accurate but more complex characterization of at-risk households would help in formulating practical and easy-to-remember prevention guidelines.

The secondary attack rate for HUS among siblings in this outbreak of STEC O157 infection was 4%, indicating that a case of STEC O157 infection in a child should be considered to be a medical emergency. By comparison, the secondary attack rate is estimated to be 10 times lower for meningococcal disease (data not shown). Finally, we were not able to obtain more-detailed exposure information about households that might have allowed us to more precisely characterize the circumstances in which secondary transmission had occurred. However, clinicians in general practice are already flooded with guidelines [29], and therefore, it is debatable whether using a more accurate but more complex characterization of at-risk households would help in formulating practical and easy-to-remember prevention guidelines.

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Acknowledgments

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References


