Isolation of Patients Acutely Infected with *Escherichia coli* O157:H7: Low-Tech, Highly Effective Prevention of Hemolytic Uremic Syndrome

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(See the article by Werber et al. on pages 1189–96)

Ponder this scenario: you are evaluating a 2-year-old boy who has just presented with bloody diarrhea to the emergency department of your hospital. His diarrhea began 72 h before presentation and became bloody 3 h before presentation. He has had 7 bowel movements in the past 24 h. His mother reported an axillary temperature of 39.0°C on the first day of illness, but he has had no fever since then. He has been urinating at least every 6 h. His abdominal pain is worse around the time of defecation. His father, mother, 1-year-old sister, and 4-year-old brother are healthy. His mother reports that they were at a petting zoo in another state a week before presentation, and she had heard that one of the visitors to that zoo was in the hospital with kidney failure and that several other visitors also had bloody diarrhea.

The boy has vomited intermittently since the illness began but keeps down a cup of juice offered to him in your presence. He is afebrile, appears to be well hydrated, and has diffuse abdominal tenderness, but the rest of his examination parameters are normal. His WBC count is 12,100 cells/mm³, with an unremarkable differential (i.e., the relative “bandemia” characteristic of *Shigella* infections is not present). His platelet count is 380,000 platelets/mm³, his hematocrit is 39%, his creatinine level is 0.4 mg/dL, and his blood urea nitrogen level is 8 mg/dL. A stool sample is sent for culture for *Campylobacter jejuni*, *Escherichia coli* O157:H7, *Salmonella* species, *Shigella* species, and *Yersinia* species. The laboratory notes that there are few polymorphonuclear leukocytes in the submitted stool sample. The lack of a fever in a medical setting prompts you to consider that this child has an *E. coli* O157:H7 infection, and the time course, physical examination findings, and available laboratory test results are all consistent with this pathogen as the cause of his symptoms. The history of the illnesses at the petting zoo reinforces your opinion that this is an *E. coli* O157:H7 infection, and the time course, physical examination findings, and available laboratory test results are all consistent with this pathogen as the cause of his symptoms. The history of the illnesses at the petting zoo reinforces your opinion that this is an *E. coli* O157:H7 infection, and the time course, physical examination findings, and available laboratory test results are all consistent with this pathogen as the cause of his symptoms.

If such a patient is admitted to a hospital, that institution will no doubt apply contact precautions. Contact precautions are stringent. The American Academy of Pediatrics *Red Book* [7] recommends, for example, hospitalizing the patient in a single room, using gloves at all times, and wearing gowns during contact with an infected patient, environmental surfaces, or items in the patient’s room. If a person even enters this patient’s room, he or she will have to wear a gown. These precautions are all in addition to hand hygiene. It is unreasonable to expect families to implement measures that even be-
gin to approximate such hygienic standards at home.

Other factors favor hospital admission for infection-control purposes. Caregiver fatigue must be considered, because infected children are often awake for much of the night, because they are in pain. Exhausted parents might be less able to adhere to sanitary practices. Young children often have siblings at home, and children are the group at highest risk of developing HUS if they become infected. Among enteric pathogens in the developed world, _E. coli_ O157:H7 is singularly virulent. Even though many other pathogens, such as rotavirus, obligate contact precautions in hospitals, patients infected with these pathogens are routinely and appropriately discharged from emergency departments, with minimal consequences for others in their community.

The Wales Communicable Disease Surveillance Centre provides strong data in support of admitting to the hospital patients with symptoms indicative of _E. coli_ O157:H7 infection. They analyzed 89 households in which at least 1 patient with a primary case of _E. coli_ O157:H7 infection stayed during an outbreak in the United Kingdom and calculated the total number of patients at risk of secondary transmission. Cases were chosen in a manner that was intended to greatly reduce the possibility of including coprimary infections, which are difficult to differentiate from secondary infections. Secondary infections due to _E. coli_ O157:H7 are not rare; in outbreaks, 10% of cases have been categorized as secondary infections [8], despite widely publicized admonitions about the highly contagious nature of these illnesses. However, until the article by Werber et al. [2], it was not known exactly how large of a risk secondary spread truly is in households with a child infected with _E. coli_ O157:H7.

There are many assumptions made by Werber et al. [2] that could limit the accuracy of their estimates, but they discuss these quite well. They focus on the number of patients who would need to be isolated to prevent 1 case of HUS and were not as concerned about preventing cases in patients who did not develop this complication. Such an analysis would be useful, because preventing secondary cases in patients who do not develop HUS could offset some of the cost to the medical system from hospitalizing primary case patients. Also, the authors’ data are somewhat biased toward households with children, who are, presumably, at a greater risk of contracting a secondary infection. In addition, the authors’ work pertains to the transmissibility of an outbreak strain, and the risk might differ for sporadic primary infections or for other outbreak strains.

Despite these small limitations, Werber et al. [2] have done an admirable job of quantifying the risk of secondary cases of _E. coli_ O157:H7 infection resulting from primary case patients remaining in the community during acute illness. By the authors’ calculations, such patients are at least as hazardous as children with meningococcal disease. Therefore, it is important to heed the disease control lessons from this study and the complementary findings of Seto et al. [9], who modeled data from the 2006 United States nationwide outbreak of _E. coli_ O157:H7 infection acquired from spinach [10]. Even though person-to-person spread of _E. coli_ O157: H7 infection has occurred in hospitals [11], such transmissions are considerably less common than community-acquired secondary transmissions. It is also sobering to remember that the tragedy of the 1993 multistate epidemic of _E. coli_ O157: H7 infection was compounded by the fact that 2 of the 4 childhood fatalities occurred in children who had secondary infections [8].

When enteric pathogens pass through humans, their virulence is not only retained but might be augmented. _Vibrio cholerae_ is more infectious to mice after passage through the human gut [12]. Lombardo et al. [13] recently profiled up-regulated _V. cholerae_ genes, including virulence loci, induced in human volunteer studies. Nelson et al. [14] studied the composition of fecal specimens from patients naturally infected with cholera in Bangladesh and identified subsets of shed _V. cholerae_ that were more likely to be transmitted to household contacts. Pathogen modulation at the genomic level occurs during the course of Shiga toxin–producing _E. coli_ infections in humans [15, 16], and virulence-associated loci are well expressed [17] in _E. coli_ O157:H7 shed by children.

Postsymptomatic children who shed _E. coli_ O157:H7 are excluded from day care centers [18]. However, we do not believe that contact precautions should be implemented in this situation, because the concentration of pathogen in stool after diarrhea ceases is generally several logs lower than the concentration during acute illness, and there is less fecal output during the convalescent phase. Moreover, _E. coli_ O157:H7 persists only temporarily in human populations, even when it is disseminated in massive outbreaks [19, 20].

The prevention of even 1 secondary infection leading to HUS justifies hospitalizing many additional infected children while they are acutely ill, the added benefit of parenterally hydrating such children notwithstanding. The vascular injury that presumably precedes and leads to renal injury following _E. coli_ O157:H7 infection is already well underway by the time such patients present for medical attention [3, 21, 22]. Biologic interventions directed at children who are already symptomatic are, therefore, less likely to be successful. However, a simple infection-control measure, such as isolation, can now be implemented by aware physicians, with the goal of preventing HUS in children in the community who are not yet infected. Such an action is analogous to nonpharmaceutical interventions, such as school closures, quarantines, and banning public gatherings, which are being considered as countermeasures against hypervirulent influenza on the basis of data from the 1918–1919 pandemic [9].

Because these studies are necessarily ob-
servational and are not subject to random-
ized trials of efficacy, it will be important to
repeat the work of Werber et al. [2] in addi-
tional populations. Also, it is often challenging to identify patients with E. coli
O157:H7 infection, which is, in reality, a
rather rare event in ambulatory practice.
Point-of-care microbiologic examination
that can detect this agent and other enteric
pathogens that cause similar symptoms
would greatly assist the decision to admit
the patient to the hospital at presentation.
However, until then, we should carefully
consider the compelling empirical data
from Werber et al. [2] in favor of the com-
mon sense practice of quarantine (by hos-
pital admission) of all patients with plau-
sible or definite E. coli O157:H7 infection
during acute illness. As has often been
noted, the best way to prevent HUS is to
prevent the infections that lead to this po-
tentially lethal complication, and Werber
et al. [2] have provided 1 such prevention
strategy.

Acknowledgments

Financial support. Doris Duke Clinical Re-
search Foundation (to C.K.A.).

Potential conflicts of interest. All authors: no
conflicts.

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