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Shiga Toxin-Producing *Escherichia coli*: Burden and Trends

Shiga toxin-producing *Escherichia coli* (STEC) are a leading cause of bacterial foodborne illness in the United States. The most common STEC, STEC O157, has been estimated to cause 73,000 illnesses annually in the United States, resulting in 2,168 hospitalizations and 61 deaths[1]; however, there are more than 100 other types of STEC, known as the non-O157 STEC, that can also cause human illness. Non-O157 STEC O26, O111, and O103 are commonly associated with human disease. STEC infections can lead to bloody diarrhea and 5-15% of patients develop hemolytic uremic syndrome (HUS), which is the leading cause of kidney (renal) failure in children.

People get infected with STEC O157 in a number of ways but most illnesses are associated with eating undercooked ground beef. Recent outbreaks of STEC O157 have also been caused by eating contaminated leafy green vegetables such as spinach and lettuce, and contact with animals in settings such as at petting zoos. STEC infections can also be transmitted from person-to-person, which happens occasionally in families and child care settings. Less is known about how people get infected with non-O157 STEC but in appears that these infections may be acquired in similar ways.

STEC O157 has been a nationally notifiable disease since 1994. From its inception in 1996 through 2004, FoodNet reported a steady decrease in the incidence of STEC O157 cases, from 3 per 100,000 population in 1996 to 0.9 in 2004. In both 2005 and 2006, however, the incidence of STEC O157 infections increased, with an incidence of 1.3 cases per 100,000 population reported in 2006[2]. The reasons for these increases in STEC O157 incidence are unknown. While FoodNet has documented progress towards achieving the Healthy People 2010 goal for STEC O157 of 1 case per 100,000 population[3], these recent increases reemphasize the importance of food safety and educational efforts.

Much less is known about non-O157 STEC. Non-O157 STEC have been nationally reportable since 2000 and the number of cases reported to FoodNet has increased steadily each year since then. In part, this increase may be due to wider usage of Shiga toxin testing and changes in laboratory practices. From 2000 through 2006 the incidence of non-O157 STEC reported in FoodNet sites increased nearly four-fold, from 0.12 cases per 100,000 population to 0.42 cases per 100,000 population. Considerable geographic variation is also seen for non-O157 STEC, with an incidence rate ranging from 0.15 cases per 100,000 population in Georgia to 1.02 cases per 100,000 population in New Mexico. Much more work is needed to understand the epidemiology of non-O157 STEC.

FoodNet surveillance for STEC is essential for measuring trends and monitoring the burden of STEC infections in the United States. Recent increases in STEC O157 coupled with our increasing understanding of the importance of non-O157 STEC underscore the need for renewed focus on effective prevention and control measures. More information on STEC is available at www.cdc.gov/ecoli.

—Hannah Gould, CDC FoodNet Team

Image courtesy of FSIS webpage: http://www.fsis.usda.gov/images/thermometer_in_burger_cutout.jpg

[1] Mead, P. S., L. Slutsker, V. Dietz, L. F. McCaig, J. S. Bresee, C. Shapiro, P. M. Griffin & R. V. Tauxe. Food-related illness and death in the United States. Emerging Infectious Diseases. 1999:5, 607-625.

[2] www.healthypeople.gov

[3] Preliminary FoodNet data on the incidence of infection with pathogens transmitted commonly through food—10 states, 2004. MMWR. April 13, 2007:56(14); 336-339.

WHAT IS FOODNET?

The Foodborne Diseases Active Surveillance Network (FoodNet) is the principal foodborne disease component of CDC's Emerging Infections Program. FoodNet is a collaborative project of the CDC, ten sites (CA, CO, CT, GA, MD, MN, NM, NY, OR, TN), the U.S. Department of Agriculture (USDA), and the U.S. Food and Drug Administration (FDA).

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Risk Factors for Shiga Toxin-Producing *Escherichia coli*

Shiga toxin producing *Escherichia coli* O157 (STEC O157) is a bacterium that causes acute gastroenteritis with abdominal cramps and profuse, often bloody, diarrhea. About 8% of those infected go on to develop hemolytic uremic syndrome (HUS), a potentially life threatening condition resulting in acute renal failure, anemia and thrombocytopenia. Contaminated food in the United States is thought to be the main route to infection.

In 1996, the US Department of Agriculture's Food Safety and Inspection Service published the Pathogen Reduction and Hazard Analysis and Critical Control Point Systems (HACCP) regulations, which were designed to reduce bacterial contamination of meat and poultry sold in the US. When HACCP regulations were first implemented in 1998, the Centers for Disease Control and Prevention's Foodborne Diseases Active Surveillance Network (FoodNet) conducted a case-control study of sporadic (non-outbreak) STEC O157 cases and identified ground beef and farm visits as sources of sporadic infection[1].

A subsequent FoodNet case-control study was conducted in 1999-2000[2]. This study focused on identification of risk factors for sporadic STEC O157 infections in Connecticut, Georgia, Minnesota, Oregon and selected counties in Maryland, California and New York. The study area covered about 11% of the U.S. population and included 283 patients infected with STEC O157 and 534 healthy controls. The patients and controls were interviewed by telephone and asked about exposures to food, water and animals in the seven days before illness began.

STEC O157 infection was associated with eating undercooked (pink) hamburgers, drinking untreated water from ponds, lakes, rivers or streams, and contact with cattle, by either living, working on, or visiting a farm. Infection was not associated with eating in restaurants, or purchasing meat from custom slaughter houses. This study also showed a protective effect of a diverse diet that was high in fruits and vegetables. Although contaminated produce has caused outbreaks of STEC O157, the benefits of a diet high in fruits and vegetables appear to outweigh the potential risk of consuming produce that may be contaminated with STEC O157.

Most study participants were aware of and practiced proper food safety techniques. The vast majority washed their hands and food preparation areas while preparing meat. About half of respondents placed ground beef into separate plastic bags at the grocery store before putting the meat into the cart with the other groceries. In spite of knowing proper techniques, consumption of undercooked ground beef continued to be an important route of infection in 2000. Only 2-3% of participants cooked with a meat thermometer to determine proper cooking temperatures, and education of consumers remains an important deterrent to infection.

-Karen Edge, New Mexico Department of Health

[1]Kassenborg HD, Hedberg CW, Hoekstra M, Evans MC, Chin AE, Marcus R, Vugia DJ, Smith K, Ahuja SD, Slutsker L, Griffin PM; Emerging Infections Program FoodNet Working Group. Farm visits and undercooked hamburgers as major risk factors for sporadic Escherichia coli O157:H7 infection: data from a case-control study in 5 FoodNet sites. Clin Infect Dis. 2004 Apr 15;38 Suppl 3:S271-8.

[2]Voetsch et al. Risk Factors for Shiga Toxin-Producing Escherichia coli O157 Infections in FoodNet Sites, 1999-2000. Epidemiol and Infect. 2007 Vol 134(6); 993-1000.

Genetic Predictors of HUS Among Persons Infected with *E. coli* O157

Shiga toxin-producing *Escherichia coli* O157 (STEC O157) causes an estimated 73,000 illnesses annually in the United States, resulting in 2,168 hospitalizations and 61 deaths. Approximately 5-15% of persons infected with STEC O157 develop hemolytic uremic syndrome (HUS), the leading cause of renal failure in children. In 2007, FoodNet launched a study to identify human genomic factors associated with the development of HUS among persons infected with STEC O157.

All STEC O157 cases ascertained through FoodNet surveillance from 2006 to 2008 will be mailed a kit asking them to submit a mouthwash sample for DNA testing for polymorphisms and mutations in candidate genes. Medical chart review will be used to document if cases develop HUS, defined as a clinical diagnosis of HUS by a physician with the detection of STEC O157 as the causative agent by culture, serology, EIA, or PCR. The DNA profile of persons infected with STEC O157 who develop HUS will be compared to those without a HUS diagnosis to identify genetic variants.

To date, 37 persons have been enrolled and an additional 40 persons have agreed to participate. Many FoodNet sites only recently received IRB approval, and as they have begun the number of specimens submitted is rising sharply. DNA has been successfully isolated from almost all specimens submitted thus far.

This ongoing study is one of the first to look at human genomic factors associated with a food-borne pathogen. Identification of genetic factors associated with HUS will contribute to a better understanding of the pathogenesis of HUS and will have potential therapeutic and preventive implications[1].

-Abstract by Hannah Gould et al., CDC FoodNet Team

[1]Gould et al. Genetic Predictors of Hemolytic Uremic Syndrome Among Persons Infected with Escherichia coli O157. Accepted for poster presentation at CDC Celebrates 10 Years of Public Health Genomics; Translating Gene Discoveries into Population Health Benefits. Jan 2008.

Recent Changes in STEC Laboratory Practices: the FoodNet STEC Laboratory Survey

Shiga toxin-producing *Escherichia coli* O157:H7 and other strains of *E. coli* that produce Shiga toxin are known collectively as Shiga toxin-producing *E. coli* (STEC). STEC strains are an important cause of sporadic and outbreak-associated diarrhea in the U.S. STEC O157 is the only STEC which can be readily detected by culturing on sorbitol MacConkey agar and the most commonly reported STEC strain in the U.S. The incidence, trends, and epidemiology of non-O157 STEC are not well described. In 2000, non-O157 STEC infections became nationally notifiable. Since then, the number of non-O157 STEC infections has been increasing in FoodNet sites since it became reportable. However, the number of cases reported by year and site may be partly due to differences and changes in laboratory practices.

The Centers for Disease Control and Prevention outlined the public health importance of identifying all serogroups of STEC from patient specimens in the September 29, 2006 issue of the Morbidity and Mortality Weekly Report (MMWR, Vol. 55, No. 38) . Highlighted in this article were best practices for identifying all STEC infections. Screening all stool samples submitted for routine enteric bacterial testing for Shiga toxins using enzyme immunoassay (EIA) or polymerase chain reaction (PCR) and culturing simultaneously for *E.coli* O157 would facilitate the rapid diagnosis and treatment of patients with STEC infections. Also included in the MMWR article were recommendations for clinical laboratories to submit all positive Shiga toxin stool specimens to the state public health laboratory for isolation and identification of any O157 or non-O157 STEC from a patient specimen.

In the spring of 2007 FoodNet evaluated adherence to these published guidelines, as well as changes over time in clinical laboratory practices to better understand STEC surveillance trends. All clinical laboratories serving the ten FoodNet sites were surveyed about their methods for identifying STEC. The surveys were conducted in person, by telephone, or via a web-based survey tool. The survey addressed standard operating procedures related to culture and non-culture-based laboratory methods. A similar survey was conducted by FoodNet in 2003. We were able to compare the results of the two surveys to examine changes over time in testing practices. Responses to the 2007 survey were received from 668 (99%) of 675 labs serving the ten FoodNet sites. Of these, 433 (65%) tested on-site for STEC O157. Preliminary results indicate that between 2003 and 2007 the percentage of clinical laboratories utilizing a method that would detect STEC strains other than O157 increased from 2% to 10%. The 2007 survey also found that only 2% of the labs reported simultaneously using non-culture and culture based methods as recommended in CDC guidelines. However, among laboratories using non-culture methods, 62 (94%) sent a specimen or clinical material on to the state public health laboratory for further testing as recommended by the guidelines.

Laboratory methods for the identification of STEC are rapidly changing. It is important to monitor these changes and ensure that proper diagnostics are being conducted. Barriers to following published guidelines should be explored to improve the identification of STEC. Rapid identification and subtyping is important to determine serotype specific trends of STEC and for the timely detection of outbreaks.

—Dina Hoefer, New York State Department of Health

Spotlight on STEC Outbreaks

Outbreaks of STEC O157 are most commonly associated with the consumption of raw or undercooked beef products. However in 2006, three large national outbreaks of STEC O157 were associated with the consumption of raw produce. The first outbreak occurred in August of 2006, and infections were associated with the consumption of bagged baby spinach. Two outbreaks occurred in November of 2006 and infections were associated with the consumption of shredded lettuce at two unrelated Taco Chains with separate lettuce suppliers and growers.

These STEC outbreaks were compared to leafy greens outbreaks reported to CDC's Electronic Foodborne Outbreak Reporting System (eFORS) from 1995-2005. During the 2006 outbreaks, an estimated 362 persons were ill, 183 (51%) were hospitalized, 41 (11%) developed Hemolytic Uremic Syndrome (HUS), and 3 (<1%) died. In comparison, from 1995 to 2005, there were 26 STEC O157 outbreaks due to leafy greens with a total estimated ill of 751, 94 (8%) hospitalized, 2 (<1%) developed HUS, and 1 (<1%) died. The vehicles in these 26 outbreaks were unspecified lettuce (n=13), mesclun/mix (n=2), cabbage (n=3), spinach (n=1), iceberg (n=2), romaine (n=3), and other leafy (n=2).

Recent outbreaks associated with fresh produce, and leafy greens specifically, illustrate that vehicles for STEC O157 other than raw or undercooked beef are of increasing importance. Identifying and controlling routes of contamination for produce poses a new and unique challenge for food safety. Public health response to foodborne outbreaks associated with produce will require innovative and new strategies for surveillance and prevention[1].

—Matt Biggerstaff, CDC OutbreakNet Team

Between 2004 and 2006 , there were 1915 STEC cases in FoodNet; of which 281 (14.7%) were outbreak-associated.

[1]Nguyen, T. Lettuce and Leafy Greens: Connecting the Dots on Epidemiologic Investigations. Presentation at the 94th Annual Meeting of the International Association for Food Production, Lake Buena Vista, FL, 2007.

Update from FSIS-FDA-CDC non-O157 STEC Meeting

A public meeting on "The Public Health Significance of non-O157 Shiga Toxin-Producing *Escherichia coli*", jointly sponsored by FSIS, FDA and CDC, was held at George Mason University, Arlington, VA, October 17th, 2007. Patricia Griffin, Phillip Tarr and Sharon Hurd presented updates on the epidemiology of non-O157 STEC, stating that while certain specific serotypes, including STEC O26, O45, O103, O111, O121 are of concern, STEC O157 posses the single greatest threat to public health. Cheryl Bopp and Peter Feng discussed the difficulties faced when testing for non-O157 STECs, which lack the unique biochemical characteristics that make isolation of STEC O157 relatively straightforward. Mohammad Koohmaraie and Hussein Hussein discussed ongoing research and beef industry outreach efforts, noting that while 5.8% of US ground beef surveyed contained the top six serotypes of concern identified by CDC, no meatborne non-O157 STEC outbreak has been identified in the US. Flemming Scheutz and Martina Bielaszewska went on to present information on European outbreaks, where these organisms appear to pose a greater public health burden. Phil Derfler and Robert Buchanan, representing policy makers in FSIS and FDA respectively, addressed the regulatory difficulties associated with the control of non-O157 STEC in food, and promised to continue to seek viable options.

The public meeting provided the opportunity for subject matter experts and stakeholders to discuss the increasing clinical evidence that some non-O157 STECs are significant human pathogens and the dearth of food attribution information, largely stemming from the lack of specific assays. Although there are gaps in current knowledge, which have hampered the development of appropriate regulatory controls, there was general agreement that this proactive meeting was very timely, and should result in the further scientific review of these organisms and appropriate measures to address them.

The white paper, presentations and transcripts are available on the FSIS website: http://www.fsis.usda.gov/.

—Denise Eblen, USDA FSIS.

RECENTLY PRESENTED FOODNET ABSTRACTS AT IDSA

- Barton-Behravesh C. et al. Multistate Outbreak of *Salmonella* Typhimurium Infections Associated with Consumption of Restaurant results of 243 *Listeria monocytogenes* isolates from patients in the USA, 2000-2005.
- Edge, K. et al. Increase in Shiga Toxin-producing *Escherichia coli* (STEC) in New Mexico, 2004-2006.
- Long, C. et al. Decline in *Yersinia enterocolitica* infections in FoodNet, 1998-2006.
- Henao, O. et al. Trends in the incidence of Shiga toxin-producing *E. coli O157* infections. Foodborne Diseases Active Surveillance Network, 1996-2006
- Mickelson, S. et al. *Salmonella* Bacterium in FoodNet Sites, 1996-2006.
- Moyer, L. et al. National Incidence of Hospitalization of Patients with *Campylobacter*, *Listeria* and *Salmonella* Infections, 1998-2004.
- Ong, L. et al. Trends in Incidence of Hemolytic Uremic Syndrome, Foodborne Diseases Active Surveillance Network 2000-2005.
- Patrick, M. et al. Age and Gender Trends in Incidence of Sporadic *Campylobacter* Infections, FoodNet, 1996-2006.
- Scallan, E. et al. Burden of Acute Gastrointestinal Illness among Immunocomprimised Persons.

RECENTLY PUBLISHED FOODNET MANUSCRIPTS

- Majowicz, S. et al. A common, symptom-based case definition for gastroenteritis. Epidemiol and Infect; Published online by Cambridge University Press 9 Aug 2007.
- Marcus, R. et al. Re-assessment of Risk Factors for Sporadic *Salmonella* Enteritidis Infections: A Case-Control Study in Five FoodNet Sites, 2002-2003. Epidemiol and Infect; 2007. Vol 135(1): 84-92.
- Samuel, M. et al. Consumption of Risky Foods Among Adults at High Risk for Severe Foodborne Diseases: Room for Improved Targeted Prevention Messages. J. of Food Safety; 2007. Vol 27(2): 219-32.

Additional Resources on STEC

- http://www.cdc.gov/ecoli/
- http://www.fsis.usda.gov/food_safety_education/ask_karen/index.asp#Question (Enter "E. coli")

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