

Verotoxigenic *Escherichia coli* (VTEC) Infection



Verotoxigenic *E. coli* is also referred to as verotoxin-producing *E. coli*, enterohaemorrhagic *E. coli* (EHEC), Shiga toxin-producing *E. coli* (STEC) and verocytotoxin-producing *E. coli*. The most widely recognized serotype within this group of pathogens is O157:H7 (1).

Case Definition

Confirmed Case:

- Isolation of verotoxin-producing *E. coli* OR identification of verotoxin from a stool specimen (2).

Clinical Case:

- Clinical illness characterized by liquid or bloody diarrhea and abdominal cramps in a person who is epidemiologically linked to a confirmed case (2). Illness may be complicated by hemolytic uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP) or pulmonary edema with no other identifiable cause (2).

Reporting Requirements

- All stool specimens that are culture-positive for *E. coli* O157:H7, verotoxin-producing *E. coli*, or from which verotoxin is identified are reportable by laboratory to the Communicable Disease Control Unit, Manitoba Health.
- All confirmed cases of VTEC are reportable by the attending health care professional to the Communicable Disease Control Unit, Manitoba Health.
- Cases of HUS whether or not associated with VTEC are reportable by the attending health care professional to the Communicable Disease Control Unit, Manitoba Health.

Clinical Presentation/Natural History

The human response to VTEC inoculation ranges from asymptomatic infection to non-bloody diarrhea, hemorrhagic colitis (bloody diarrhea), HUS and death (3, 4, 5). After ingestion of the

organism, the bacteria colonize the intestine and secrete cytotoxin(s), which can act locally or systemically (6, 7). Illness with VTEC organisms typically begins with abdominal cramps and non-bloody diarrhea, that usually progresses to bloody diarrhea (3, 8-10). Nausea and vomiting may also occur (7, 11, 12). Fever is less common (4, 9, 10, 13), reported in less than one-third of cases (8). The frequent absence of fever may lead to non-infectious diagnoses, such as intussusception, ischemic colitis, hemorrhage and inflammatory bowel disease (5, 6). Symptomatic illness is usually self-limiting and lasts four to eight days on average (11, 14-17).

The most severe clinical manifestation of VTEC infection is HUS (8), defined as a combination of renal failure, low platelet count and hemolytic anemia (1, 3, 18). The HUS presentation is sometimes diagnosed as TTP in adults (8). Approximately four to eight per cent of *E. coli* O157:H7 cases progress to HUS (13, 19). The percentage of non-O157:H7 VTEC cases that result in HUS is unknown (20). HUS can cause neurological complications such as seizure, stroke and coma in 25 per cent of patients and chronic renal sequelae, usually mild, in approximately 50 per cent of survivors (12). Complications are most common in children under five years of age and the elderly (21-23). The case fatality rate for patients with HUS is approximately three to five per cent (12, 22).

Etiology

E. coli O157 is a short, rod-shaped, gram-negative bacterium that is resistant to acidic conditions, dehydration and high salt concentrations (24). These characteristics help it to survive at numerous points in processing, from farm to human ingestion (24). *E. coli* O157:H7 is the most common of the *E. coli* serovars identified in humans with VTEC infection, in Canada (25). However, more than 100 serotypes of *E. coli* have been shown to produce verocytotoxin(s) (26). *E. coli* O157:H7 is so-named

because it expresses the 157th somatic (O) antigen identified, and the seventh flagellar (H) antigen (5). Other VTEC serotypes, including O26:H11, O111:NM and O103:H2 have been implicated as the cause of both outbreaks and sporadic cases of bloody diarrhea and HUS (1). *E. coli* O145 has emerged as one of the most important non-O157 serogroups associated with diarrhea and HUS in Europe (27).

Epidemiology

Reservoir: Asymptomatically colonized cattle are the main reservoir for *E. coli* O157:H7 (1, 3, 13, 24, 26, 28, 29). Beef may be contaminated during slaughter (3), and the process of grinding beef may transfer pathogens from the surface of the meat to the interior (7, 30). Other ruminants as well as wild animals (e.g., deer) have been reported to carry these organisms in their intestinal tracts (1, 3). VTEC organisms have been isolated from the feces of sheep, pigs (31) and goats (32, 33). Survival of these bacteria for several months in manure and water trough sediments has been documented (12). Recent evidence has indicated that house flies carry virulent *E. coli* O157:H7 in the farm environment, and may play an important role in the transmission of this pathogen among individual cattle as well as potentially to the surrounding farm and urban environments (24). Humans represent a reservoir for person-to-person transmission (13).

Transmission: Transmission of *E. coli* O157:H7 usually occurs through food, particularly inadequately cooked ground beef (3, 19, 34-36). Transmission through ingestion of other contaminated foods such as alfalfa sprouts (37, 38), apple cider (16), salami (39), spinach (40), lettuce (10), unpasteurized milk (3, 6, 19) and cooked, sliced meat (41) has been documented. Contamination of these foods may occur when they come into contact with feces from domestic or wild animals at some stage during cultivation or handling (12). Infected produce may also result from cross-contamination during food preparation (19).

Waterborne transmission, by drinking contaminated water (19, 42), does occur. A large outbreak of *E. coli* O157:H7 associated with an improperly treated municipal water supply occurred in Walkerton, Ontario (43). Outbreaks of *E. coli* O157:H7 have been associated with bathing at a public beach (44), a children's water spray park (45), and an improperly chlorinated swimming pool (17).

Transmission through direct contact with farm animals such as in petting zoos occurs, though less frequently than through other known routes (19, 32, 33, 46, 47).

Secondary spread by person-to-person transmission occurs through the fecal-oral route (12), particularly in families (11, 22), child care centres (19, 21, 48), personal care homes (26, 49) and other institutions (50).

Occurrence:

General: VTEC infections have been reported in North America, Europe, Japan, South Africa, Australia and the southern cone (area below Tropic of Capricorn) of South America (13). The burden of illness from HUS is comparable between Australia, North America and Europe (3). As well, the association between HUS cases and *E. coli* infection is similar in various parts of the world (3). The annual incidence of infection with VTEC ranges from one to 30 cases per 100,000 population in industrialized countries (5, 18). Data on the situation in developing countries are limited, as surveillance for this pathogen is not done routinely (12). *E. coli* O157:H7 causes both sporadic and epidemic infections. However, sporadic cases of *E. coli* O157:H7-associated disease account for the vast majority of infections (1, 3, 29, 51). The true incidence of infection is likely underestimated as many outbreaks go unrecognized or are not reported to public health authorities (19). The highest attack rate is among children younger than five years of age (11, 16, 18). Peak incidence occurs during the summer months (5, 9, 11, 18, 19, 24, 26).

Canada: In the year 2000, the incidence of VTEC infection was 8.81 cases per 100,000 population (52). In the past, diagnostic efforts have focused on *E. coli* O157:H7 due to its clear association with severe clinical syndromes and ease of identification as well as its association with several large, well-publicized outbreaks (53). The pre-dominance of serotype O157 is an artifact of testing and looking specifically for this serotype. The rates of VTEC infection have remained relatively constant (54).

Manitoba: There were 59 reported cases of verotoxin-producing *E. coli* in 2004, 38 reported cases in 2005 and 170 reported cases in 2006 (55). Almost 25 per cent of the cases reported in 2006 were from a large outbreak in Winnipeg associated with the consumption of ground beef (56). While many of the verotoxin-producing *E. coli* isolated from cases are serotype O157:H7, other serotypes are included as well. A large number (63 per cent of cases studied) of infections associated with non-O157 VTEC was documented in a recent Manitoba study (53). Most non-O157 cases appeared to be sporadic infections occurring in rural areas (53). Other common serotypes found in Manitoba include O26:H11, O121:H19, O103:H25 and O111:NM (53).

Incubation Period: The incubation period is usually three to four days (8, 12), but ranges from one to eight days (5, 8). The infectious dose of *E. coli* O157:H7 is low: between 50 to 1,000 organisms (6, 8, 10, 18).

Host Susceptibility and Resistance: Children are most susceptible to *E. coli* O157:H7 disease (3, 11, 12, 16, 34). The elderly are also known to be more susceptible to this infection (1, 3, 6). Individuals of all ages, however, can suffer infection from *E. coli* O157:H7 (3). Risk factors for acquisition of VTEC infection include exposure to farm animals or the farm environment (12), eating at a table service restaurant (service is provided to customer's table rather than at the counter), using immune

suppressive medication (for adults only), and obtaining beef through a private slaughter arrangement (3). Young children may also have specific risk factors including inadequate personal hygiene, habits such as nail-biting and thumb-sucking, and close contact with domestic animals and their food (26).

Period of Communicability: In humans, *E. coli* may be shed in the stool for several weeks following resolution of symptoms (5). Young children tend to carry the organism longer than do older children and adults (5). Prolonged fecal shedding (32, 48, 58, 59) and intermittent fecal shedding (57) have been documented in children. An asymptomatic carrier state has been reported, where individuals show no clinical signs of disease but are capable of infecting others (12, 32). Asymptomatic prolonged carriage is unusual (18).

Diagnosis (59, 60)

All *E. coli* O157 organisms must be referred to Cadham Provincial Laboratory for confirmation and verotoxin testing.

Biosafety level 2 containment is used when working with VTEC organisms.

An adequate history and a specific request for verotoxin testing is required on requisitions, as otherwise the laboratory diagnosis will be missed.

The laboratory protocol is that cultures are performed in sorbitol-containing MacConkey agar (SMAC) on liquid or bloody stools, stools with specific requests for verotoxin or *E. coli* O157, and stools from patients with relevant history (hemorrhagic colitis, HUS, foodborne illness (FBI), blood in stools, "hamburger disease," previous verotoxin or *E. coli* O157 positive, etc). Sorbitol-negative colonies that agglutinate O157 antisera can be presumptively identified as *E. coli* O157 (7). Due to possible cross-reactions with other sorbitol-negative organisms that agglutinate in O157 antisera, isolates are confirmed as *E. coli* using a commercially available biochemical test (59).

As verotoxin may still be detectable after VTEC is no longer recoverable by culture and as non-O157 VTEC are not likely to be detected on SMAC (as most of them ferment sorbitol), two methods are used to assay for verotoxin. Filtrates of stool specimens used for culture are assayed in tissue culture for free fecal verotoxin. In addition, verotoxin assays are performed on the bacterial growth resulting from culture of the stool sample. A specimen is positive for verotoxin if there is neutralization by the appropriate antitoxin. Cadham Provincial Laboratory retrospectively further investigates non-O157 verotoxigenic-positive isolates for epidemiological purposes.

Key Investigations

- The investigating regional health authority (RHA) should communicate with Cadham Provincial Laboratory to confirm whether or not *E. coli* O157 from referring laboratories is confirmed as such. The lab will contact the Communicable Disease Control (CDC) Unit if *E. coli* verotoxin test results are negative, and the CDC Unit will notify the investigating RHA by telephone. Since confirmation of *E. coli* O157:H7 organisms and verotoxin testing may take up to one week in some cases, preliminary reports of *E. coli* O157:H7 should be acted on as if a verotoxin-producing organism has been identified, until and unless verotoxin tests are confirmed negative.
- Explore whether there is a history of recent activities such as visiting a farm or petting zoo, swimming or playing at a water park or wading pool and foreign travel (61).
- Conduct environmental sampling (i.e., swabs to sample small surface areas such as hard toys and door knobs, and sponges to sample large surface areas such as counters) at the child care or pre-school facility in the event of an outbreak (48).
- Take a history of food and water ingestion and time of consumption.
- Conduct microbiologic analysis of food and water samples that were ingested (25), if history implicates food or drinking water as the source of illness and/or multiple cases report eating a common food item or eating at a common food establishment (62).
- Investigate the food chain when food is the suspected vehicle of infection (61).
- Screen contacts as indicated under Management of Contacts.

Control

Management of Cases:

- All cases should be instructed about disease transmission and appropriate personal hygiene (63).
- No specific treatment has been shown to decrease the severity of illness or prevent complications (20, 64).
- Prompt diagnosis and good supportive care (5, 18, 23, 65) to maintain hydration, electrolyte balance (8, 18), and nutrition are crucial (18).
- Routine practices and contact precautions are indicated for patients during acute illness (8, 13).
- Cases cared for in the home should be managed using enteric precautions (66) as detailed in *Control of Enteric Infections* in the Manitoba Health Communicable Disease Protocol Manual.
- There is no evidence demonstrating that antimicrobial therapy is beneficial and some evidence that it may be harmful (11, 22, 49, 64, 67); therefore, it is not recommended (6, 8, 65).
- As the use of antimotility agents has been associated with longer duration of symptoms (6, 49, 64), they are not recommended (6-8, 22, 65).
- During the week following onset of diarrhea, patients with confirmed VTEC infection should be monitored for signs and symptoms of HUS (5, 7, 8), such as pallor and oliguria (5, 7).

- Consideration should be given to excluding infected individuals who are employed to handle food or provide patient or child care until two stool specimens taken at least 24 hours apart are negative for VTEC (13, 61), or as directed by the Medical Officer of Health (MOH). If symptoms have resolved and hygiene is adequate, the MOH may allow a return to work without obtaining two negative stool specimens.
- Children should be excluded from child care centres until symptoms have resolved and two follow-up stool specimens taken at least 24 hours apart test negative for free verotoxin (8, 13, 21, 48, 57, 58). Follow-up stool specimens (in the context of an outbreak) must be submitted to Cadham Provincial Laboratory for testing.

Management of Contacts:

- Contacts should be instructed about disease transmission and appropriate hygiene (63).
- Contacts who are symptomatic should be assessed by a physician (63).

Food Handlers, Health Care and Child Care

Workers: If contacts are symptomatic, they should be excluded from food handling and patient/resident care until symptoms are resolved (68). Testing of asymptomatic persons is not recommended unless institutional or child care centre transmission is suspected (68).

Institutional Contacts: If the index case is a resident or staff member in a hospital or personal care home, an outbreak investigation must be carried out immediately (68). See below for management of outbreaks. It must be determined whether a common source outbreak has occurred, and immediate measures taken to identify and isolate persons who may be transmitting the infection (68).

Child Care Facilities: Person-to-person transmission of VTEC is facilitated in child care settings and attendees are in the age group where complications are more frequent (68). See below for management of outbreaks.

Management of Environment

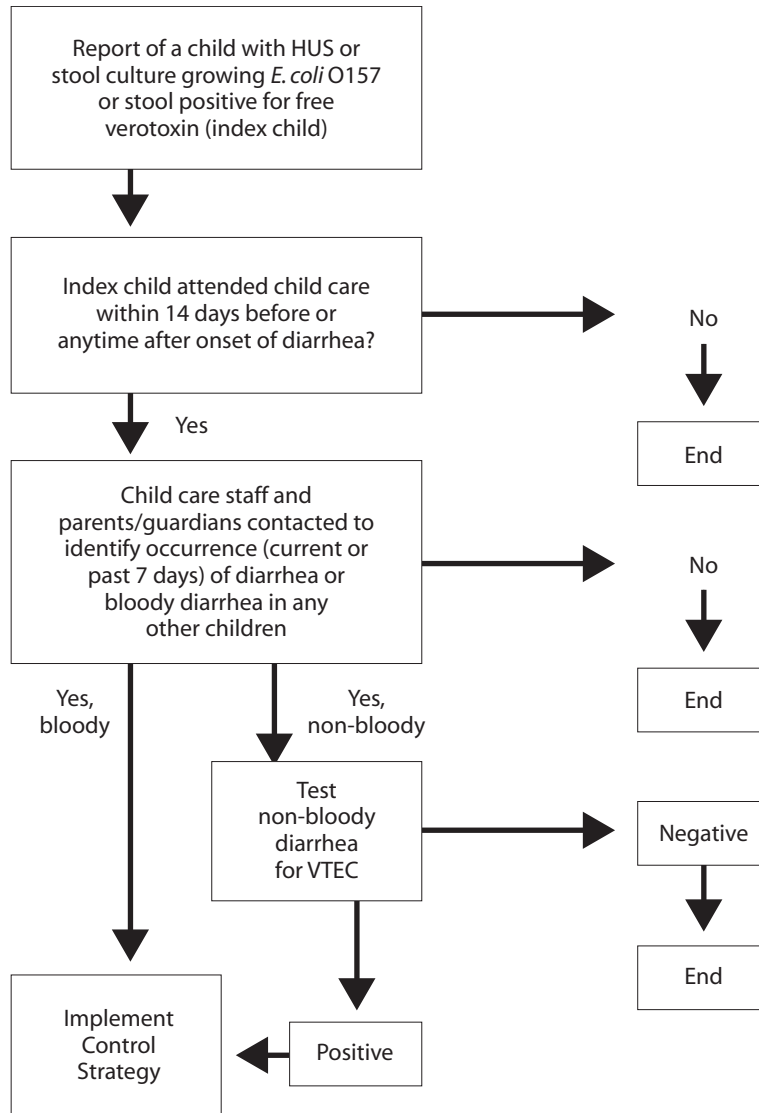
- Pasteurization of milk and juices (1, 16, 68).
- Requires control measures at all stages of the food chain; from agricultural production on the farm, to processing, manufacturing, and preparation of foods in both commercial and domestic environments (12).
- Protect drinking water sources and recreational water areas from animal wastes (12).
- Purify (i.e., chlorinate) public water supplies and swimming pools (68).
- Anyone with a diarrheal illness should avoid swimming in public pools or lakes, or sharing a bath with others (22).

Management of Outbreaks

- Health care facilities should follow established outbreak management protocols for enteric infections.
- The protocol below is based on one developed by the Minnesota Department of Health in response to outbreaks of VTEC in child care facilities. It should be initiated when a case of *E. coli* O157 infection, or HUS, or stool positive for free verotoxin is identified in a child who attends a child care facility (68).
- Transmission may be suspected in other circumstances: for example, diarrhea in siblings and parents of children attending child care, or in child care staff.

Communicable Disease Management Protocol

Evaluation of a Child Care Facility where VTEC Infection is Confirmed or Suspected

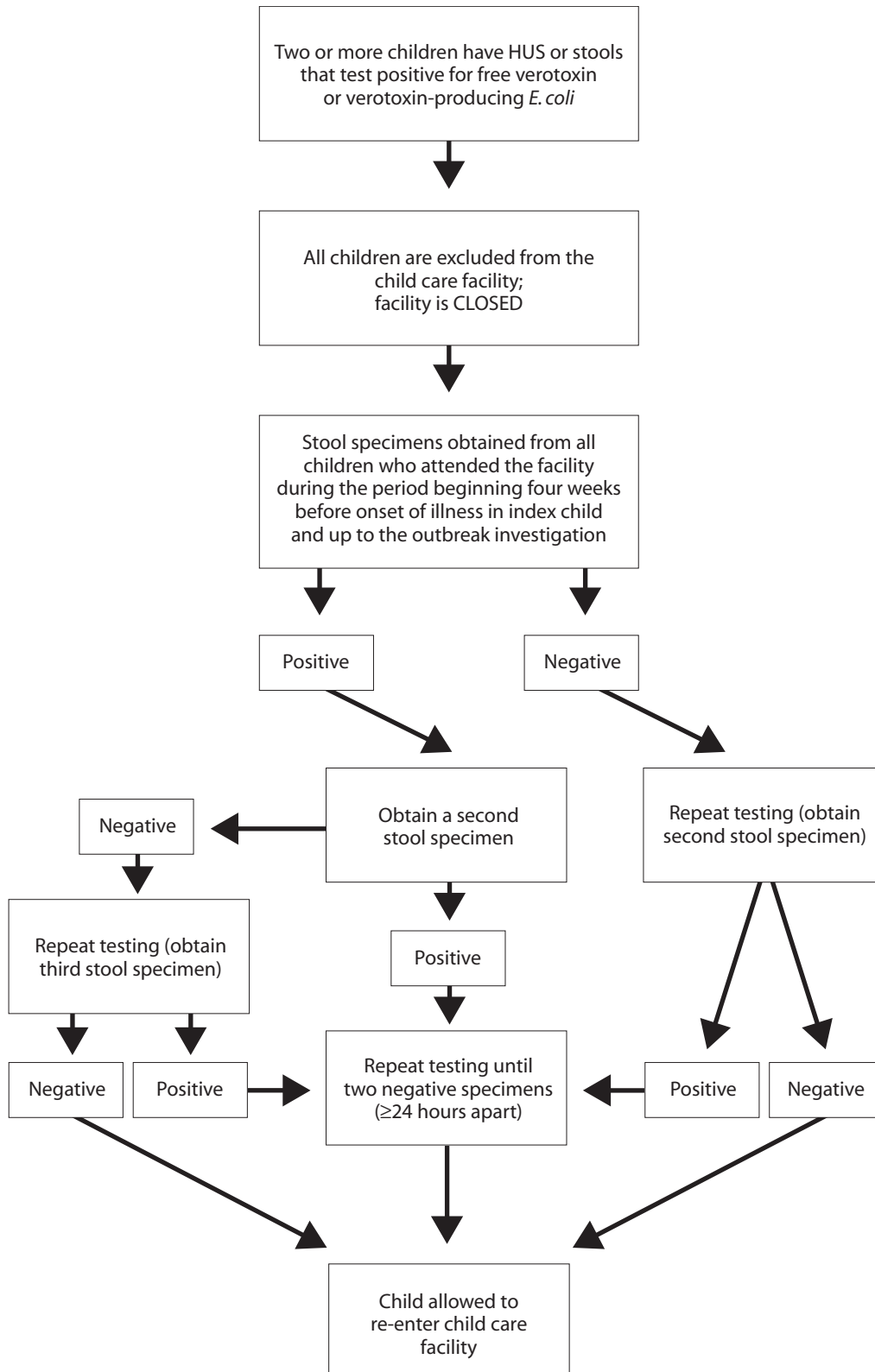


See Sample Letter A that follows

Control Strategy

- The Medical Officer of Health or designate should meet with the child care administration to review the cases and discuss control measures (68).
- Stool specimens should be obtained from all children who attended the child care facility during the time period beginning four weeks before onset of illness in the index child and up to the outbreak investigation. Stool collection and transportation should be co-ordinated by the local public health jurisdiction, with assistance from the provincial laboratory as required (68).
- If more than one child in the child care centre has been diagnosed with VTEC infection, it will be necessary to exclude all children from attending the child care setting. One of the requirements for allowing a child to re-enter child care is the provision of two stool specimens collected at least 24 hours apart that test negative for free verotoxin (8, 13, 48). These stool specimens must be submitted to Cadham Provincial Laboratory for testing.
- Children with positive stool specimens should continue to be excluded, even if asymptomatic, until two negative specimens (taken at least 24 hours apart) are obtained (8, 13, 48). Parents should be persuaded **NOT** to take their children to another child care centre (5, 21).
- A letter providing general information on *E. coli* O157 transmission and specific instructions regarding stool collection procedures and criteria for re-entry into child care should be sent to all families when the investigation is initiated. See Sample Letter B that follows.
- The Medical Officer of Health should review clinical and stool test reports and monitor re-entry to day care. The local public health jurisdiction should collect and analyze data from the outbreak investigation.
- When an outbreak of VTEC occurs in a child care facility, the Medical Officer of Health may seek to close the facility until the outbreak is over. Facility closure can end the outbreak by providing an opportunity for thorough environmental cleaning and by decreasing the potential for close contact with symptomatic children or children shedding the bacteria (48). See below for flow chart representation of implementation of a control strategy for VTEC infection in a child care facility. Positive refers to a stool specimen that is positive for free verotoxin and negative refers to a stool specimen that is negative for free verotoxin.

Communicable Disease Management Protocol



Preventive Measures:

- Screening animals pre-slaughter to reduce the introduction of large numbers of pathogens in the slaughtering environment (1).
- Education of farm workers in principles of good hygienic practice, to keep contamination to a minimum (12).
- The public should be made aware that all raw meat that they purchase is potentially contaminated; and handle it accordingly (34).
- Thorough cooking of all food derived from animal sources, especially ground beef. Cook to an internal temperature of 71°C for at least 15 seconds (69).
- Educating consumers about cross-contamination of foods and heeding warning labels (29).
- Educating consumers about contamination of food preparation environments (kitchen counters, sinks, cutting boards) and implements (meat cutting and grinding utensils, wash cloths, etc).
- The most important prevention measure in child care centres is supervised hand washing (7). Hand washing upon arrival would provide additional protection.
- A vaccine that inhibits the organism from colonizing the intestinal tracts of both cattle and humans may reflect the most promising way to prevent the infection (70). An investigational *E. coli* O157:H7 conjugate vaccine was safe and immunogenic in two to five year-old children (71).
- These vaccines are not yet licensed for human use.

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Sample Letter A: Identification of other cases of diarrhea in a child care centre after an index case has been identified (before a Control Strategy has been implemented)

Dear Parent or Guardian:

Regarding: Diarrhea due to *E. coli* O157 bacteria in your child care centre

Your public health unit is investigating the occurrence of diarrhea in the child care centre your child attends. A child has been diagnosed with a type of diarrhea caused by *E. coli* O157, commonly known as “hamburger disease.”

This infection causes diarrhea, often containing blood, with stomach cramps. In some children it may cause severe illness affecting the kidneys and blood system. It is most commonly caused by eating undercooked ground beef, but may also be spread from person to person, particularly among small children. Infected children can shed the bacteria in their stool for several weeks. Contamination of their hands with stool can allow the bacteria to spread when children handle toys and play together.

Person-to-person spread of *E. coli* bacteria is common among preschool children attending child care centres. For this reason, we would like to make you aware of the occurrence of this infection in your child care centre. If your child develops diarrhea during the next two weeks, or has been ill with diarrhea in the past three weeks, please contact your local public health unit:

Public Health Nurse: _____

Phone: _____

Address: _____

NOTE: Careful hand washing with soap and water is the key to prevent the spread of this infection from person-to-person. Good food preparation hygiene is also important.

Please do not hesitate to contact us if you have any questions or information.

Yours truly,

Medical Officer of Health

Sample Letter B: Notification of parents/guardians after a Control Strategy has been implemented in a child care centre.

Dear Parent or Guardian:

Regarding: Diarrhea due to *E.coli* O157 bacteria in your child care centre

Your public health unit is investigating the occurrence of diarrhea in the child care (facility or home) that your child attends. A specific type of bacteria known as *E. coli* O157 has been found in the stool of a child in the child care (facility or home). These bacteria often cause diarrhea with stomach cramps; blood may also be present in the stool. In some children a more severe illness known as HUS (hemolytic uremic syndrome) may occur. This illness involves the kidneys and often results in hospitalization. Fortunately, most children do not develop HUS and recover completely from their diarrhea.

The *E. coli* O157 bacteria may be found in raw meat (especially ground beef) and unpasteurized milk. Eating ground meat that is not thoroughly cooked can lead to infection. Also, the bacteria can be spread from one person to another, particularly among small children. Infected children can shed the bacteria in their stool. Contamination of their hands with stool can allow the bacteria to spread to others when the children handle toys and play together.

To determine if the infection is being spread in the child care (facility or home), the public health unit staff will be asking you a series of questions about diarrhea in your family. Since more than one child in the child care facility or home has been infected, it will be necessary to exclude all children from the child care facility or home until each child has had two stool specimens taken at least 24 hours apart that test negative for the bacteria. Therefore, the child care (facility or home) is currently CLOSED. It is important that none of the children of this care facility attend ANY other child care centre until two negative stool specimens have been obtained. This action is to prevent the further spread of bacteria to uninfected children. Although inconvenient, it is the only way to ensure the safety of the children in your child care centre and other centres.

Older children (i.e., those in school) who attend the child care (facility or home) before or after school have a lower risk of serious infection with these bacteria. However, stool specimens will be tested for *E. coli* O157 in older children as well. Older children with stool specimens testing positive for *E. coli* O157 will be excluded from attending child care centres until they have had two stool specimens taken at least 24 hours apart that test negative for the bacteria.

The investigation of this infection is being co-ordinated by your local public health unit. You will be assisted in collection of the stool samples, and can direct any questions to:

Public Health Nurse: _____

Phone: _____

Address: _____

NOTE: Careful hand washing with soap and water is the key to prevent spread of this infection from person to person. Good hygiene in food preparation is also important. Information on food safety is available from the Canadian Partnership for Consumer Food Safety Education at <http://www.canfightbac.org/en/>

Please do not hesitate to contact your public health unit if you have any questions.

Yours truly,

Medical Officer of Health