

A Canadian multicentre case-control study of sporadic *Escherichia coli* 0157:H7 infection

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OBJECTIVE: To evaluate further risk factors for *Escherichia coli* 0157:H7 infection including consumer preferences related to the consumption of ground beef and the role of person-to-person transmission of this infection.

PATIENTS AND METHODS: A case-control study of sporadic *E coli* 0157:H7 infection was undertaken in five Canadian cities from June to December 1991. One hundred cases of *E coli* 0157:H7 infection were age- and sex-matched to 200 neighbourhood controls. Cases and controls were interviewed face-to-face to obtain information on potential risk factors for infection and health outcomes. Daycare providers of case and control children were interviewed regarding risk factors for infection at the institutional level. Contacts of cases and controls who reported diarrhea in the seven days before the case onset date were also interviewed about their symptoms and risk factors.

RESULTS: All cases had diarrhea during the course of their illness and 90 (90%) reported bloody diarrhea. Four (4%) were reported to have developed hemolytic uremic syndrome; however, there were no fatalities. Sixty-one (61%) of patients were hospitalized. Two variables were associated with infection in the final conditional logistic regression model: eating pink hamburger patties (odds ratio = 12.4, P=0.0001, population attributable fraction = 40.2%) and contact with a nonhousehold member suffering from diarrhea (odds ratio = 7.0, P=0.0054, population attributable fraction = 10.3%) in the seven days before illness. Forty per cent of cases and controls who indicated that they prefer well done hamburgers said they would eat a 'pink' hamburger if served to them rather than ask that the hamburger be cooked longer.

CONCLUSIONS: Health care workers should remain vigilant in their efforts to educate the public as to the risks associated with the consumption of ground beef that is inadequately cooked, and the importance of personal hygiene in the prevention of enteric illness.

Key Words: Case-control study, *Escherichia coli* 0157:H7, Risk factors

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Étude cas/témoïn multicentrique canadienne sur une infection sporadique à *Escherichia coli* 0157:H7

OBJECTIF : Évaluer les autres facteurs de risque d'infection à *Escherichia coli* 0157:H7, y compris les préférences des consommateurs en ce qui a trait à l'ingestion du bœuf haché et le rôle de la transmission de cette infection d'une personne à l'autre.

PATIENTS ET MÉTHODES : Une étude cas/témoïn sur une infection sporadique à *E. coli* 0157:H7 a été entreprise dans cinq sites canadiens entre juin et décembre 1991. Cent cas d'infection à *E. coli* 0157:H7 ont été assortis selon l'âge et le sexe à 200 témoins du voisinage immédiat et les témoins ont été interviewés en personne afin de recueillir des renseignements sur les facteurs de risque potentiels d'infection et sur le pronostic. Les personnes responsables des enfants, témoins et cas, ont été interviewées au sujet des facteurs du risque d'infection dans les établissements de garderie. Les proches des cas et des témoins qui ont signalé une diarrhée dans les sept jours précédant la date du déclenchement de la maladie chez les sujets ont également été interrogés quant à leurs symptômes et leurs facteurs de risque.

RÉSULTATS : Tous les cas avaient présenté de la diarrhée au cours de leur maladie et 90 (90 %) ont signalé la présence de sang dans leurs selles. Quatre (4 %) ont précisé avoir développé un syndrome urémique hémolytique. Par contre, on ne dénombre aucun cas mortel. Soixante-et-un (61 %) des patients ont été hospitalisés. Deux variables ont été associées à l'infection lors du modèle de régression logistique conditionnel final : la consommation de pâtés de viande hachée encore rosée (risque relatif = 12,4; $p = 0,001$, fraction étiologique du risque = 40,2 %) et le contact avec quelqu'un ne vivant pas sous le même toit et atteint de diarrhée (risque relatif 7,0; $p = 0,0054$; fraction étiologique du risque = 10,3 %) au cours des sept jours précédant la maladie. Quarante pour cent des cas et des témoins qui avaient indiqué préférer manger des hamburgers bien cuits ont déclaré manger un hamburger dont la viande est encore rosée si on le leur sert, plutôt que de demander qu'on le fasse cuire davantage.

CONCLUSION : Les travailleurs de la santé devraient demeurer vigilants dans leurs efforts pour éduquer le public au sujet des risques associés à la consommation de bœuf haché qui n'est pas cuit suffisamment et au sujet de l'importance de l'hygiène personnelle dans la prévention des maladies intestinales.

Infection with verocytotoxigenic *Escherichia coli* 0157:H7 is widely recognized as an important cause of foodborne illness with potential life-threatening consequences (1). In Canada, between 1990 and 1995, an average of 1247 sporadic and outbreak-related cases were reported per year (2).

The majority of case-control studies related to this infection that have been published to date were conducted as part of outbreak investigations. Outbreaks have been linked to the consumption of a variety of food products including ground beef, fresh-pressed apple cider, lettuce and yogourt, the consumption of contaminated drinking water and swimming (3-9). Person-to-person transmission has been implicated in the propagation of outbreaks, particularly in daycare centres (10) and small community settings (11).

Very few population-based case-control studies of *E coli* 0157:H7 infection can be found in the literature (12-15). In a Washington State study conducted in 1985/1986, an increased risk of acquiring illness was found in those consuming rare ground beef during the week before onset (12). A Canadian case-control study of sporadic *E coli* 0157:H7 infection, conducted in 1990, identified consumption of pink ground beef and attendance at picnics or special events as significant risk factors for infection. This study (14) suggested that the majority of exposures occurred in noncommercial settings where food preparers were not formally trained and guests may have been reluctant to judge the acceptability of their host's cooking. These findings were supported by a case-control study conducted in New Jersey where an increase in sporadic cases was detected after laboratories increased testing for this bacterium (15). The present investigation was undertaken to evaluate further the risk factors for *E coli* 0157:H7 infection including consumer preferences related to the consumption of ground beef and the role of person-to-person transmission of this infection.

PATIENTS AND METHODS

The study was conducted in five Canadian cities: Vancouver (British Columbia), Edmonton (Alberta), Calgary (Alberta), Quebec City (Quebec) and Halifax (Nova Scotia). Cases were identified from among all sporadic cases of *E coli* 0157:H7 infection reported to one health unit or one public health laboratory in each of these five cities from June 4 until September 19, 1991. The public health units routinely receive case reports of *E coli* 0157:H7 infection from laboratories and physicians within their jurisdiction because infection with this agent is notifiable in Canada. Investigators at public health units also contacted the relevant diagnostic laboratories on a weekly basis during the study period to ensure that all individuals with *E coli* 0157:H7 infection were identified.

Cases were defined as persons with gastrointestinal symptoms and a positive stool culture for *E coli* 0157:H7. Patients for whom the onset date of illness occurred more than 15 days before the date of notification of the local investigator were excluded from the study.

Two neighbourhood residents matched to each case by age and sex were recruited as controls according to a standardized protocol. Infants under one year of age were excluded. Cases between one and 40 years of age were matched to controls within five years of their age. Cases over 40 years of age were matched to controls within 10 years of their age. Persons were not used as controls if they reported having diarrheal illness or gastrointestinal bleeding in the month before the interview. Controls were informed that the purpose of the interview was to obtain information as part of a study of an intestinal infection caused by a bacteria but were not told that a neighbour had suffered from diarrheal illness. No more than one participant per household was enrolled in the study.

Cases and controls were interviewed face-to-face using a standardized questionnaire regarding demographic character-

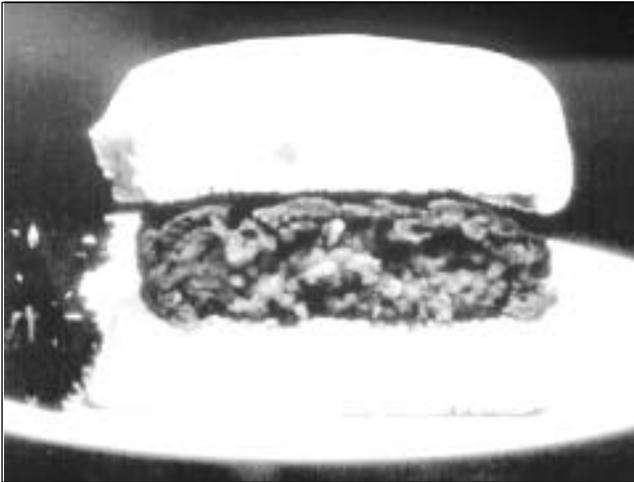


Figure 1) Photograph of 'rare' hamburger shown to study participants



Figure 2) Photograph of 'well done' hamburger shown to study participants

istics and exposure to potential risk factors for *E coli* 0157:H7 infection during the seven days before the onset of illness of the cases. The risk factors explored included contact with persons suffering from diarrheal illness; consumption, handling and preparation of ground beef and ground beef patties; consumption of other beef cuts and ground meats; consumption of other types of foods; and presence in settings where ground beef was eaten. Photographs of hamburgers cooked to varying degrees (for extremes of the range, see Figures 1,2) were shown to participants who were then asked to indicate the photograph corresponding best to the degree of cooking that they (or their child) normally prefer. Participants were also asked to indicate which photographs, in their opinion, were of inadequately cooked hamburgers.

Cases were questioned with regard to symptoms, physician visits, hospitalization and therapeutic interventions associated with the illness. Physicians of cases were interviewed to obtain information on patient symptoms and therapeutic interventions. Daycare providers of case and control children were interviewed regarding the number of children attending the daycare, the incidence of diarrheal illness among children and daycare workers before the case onset date, the role of child care providers in food preparation and food items prepared and/or consumed in the daycare during the period of concern. Contacts of cases or controls reported to have experienced diarrheal illness in the seven days before the case onset date were interviewed to obtain information on symptoms, stool culture results, beef consumption patterns and contact with persons suffering from diarrheal illness.

Data were entered into computer files and analyzed using EPI INFO 6.02 (Centers for Disease Control and Prevention, Georgia). Simple associations between case status and potential risk factors for infection were tested using Mantel-Haenszel stratified analysis. Multivariable analyses were performed using SAS version 6.09 for Unix (SAS Institute Inc, North Carolina). Variables having a significant association with infection status in the univariable analysis ($P < 0.10$) were

offered to a conditional logistic regression model using backward elimination and a forward stepwise entry procedure. The final model consisted of variables significant at $P < 0.05$. The population attributable fraction (PAF or etiological fraction) was calculated for variables in the final model (16). The protocol for this investigation was approved by the human ethical review committee of the Laboratory Centre for Disease Control, Health Canada, Ottawa, Ontario.

RESULTS

Demographics and clinical outcomes: One hundred cases and 200 matched controls were enrolled in the study as follows: Vancouver 27 cases, Calgary 30 cases, Edmonton 12 cases, Quebec City 21 cases and Halifax 10 cases. The age of patients ranged from one to 87 years (median 17.5 years). Cases comprised 56 females and 44 males. All cases had diarrhea during the course of their illness. Diarrhea occurred for a mean duration of 5.83 days (range one to 13 days) in the patients who reported that their diarrhea had stopped. Nineteen cases continued to have diarrhea at the time of the interview (mean 6.8 days). The combined mean duration of diarrhea for all patients was 6.15 days.

Ninety patients reported bloody diarrhea, and fifty-four of these reported their stool to be completely bloody. Bloody diarrhea occurred for a mean duration of 3.66 days (range one to 16 days). Three females and one male were reported to have developed hemolytic uremic syndrome (mean age 3.75 years). One patient required dialysis. No fatalities occurred. Acute medical care afforded to cases included 90 emergency room visits, 44 doctor visits, 24 walk-in clinic visits and two home visits. Sixty-one (61%) patients were admitted to hospital, although eight of these patients did not stay overnight. The average duration of hospital stay was four days (range one to 11) for the 50 patients who had been discharged from hospital when interviewed. Three patients remained in hospital at the time of their interview.

Thirty-five cases were reported by their physicians to have

TABLE 1
Variables unconditionally associated with case status (P<0.10)

Variable	Matched odds ratio	95% confidence limit of odds ratio	P
Attendance at daycare	2.87	0.87-11.00	0.0461
Contact with household member with diarrheal illness	2.55	1.07-6.20	0.0164
Contact with nonhousehold member with diarrheal illness	6.29	1.63-35.53	0.0021
Ate pink ground beef in seven days before illness	6.16	1.24-59.73	0.011
Ground beef prepared in the home in seven days before illness	0.54	0.31-0.92	0.011
Ate pink ground beef patties in seven days before illness	19.56	2.98-828.73	0.00004
Attendance at a picnic or special event where ground beef was served in seven days before illness	1.64	0.08-3.33	0.0946
Ate a hamburger cooked less than usual in seven days before illness	20.12	2.92-868.01	0.0001

received antidiarrheal agents and 37 to have received antibiotics. Physicians did not report worsening of symptoms following treatment in either group. There was no statistically significant difference between the mean duration of illness among those using antibiotics or antidiarrheals and that of those who did not.

Risk factors for infection: Variables having an unconditional association with case status (P<0.10) are shown in Table 1. Infection was not associated with manipulating ground beef with bare hands, being present in a food preparation area, consumption of casseroles containing ground beef or eating other cuts of beef or nonbeef ground meat products, even if the meat was still pink on the inside. The final conditional logistic regression model consisted of two variables: eating pink hamburger patties (odds ratio=12.4, P=0.0001, PAF=40.2%) and contact with a nonhousehold member suffering from diarrheal illness (odds ratio=7.0, P=0.0054, PAF=10.3%) in the seven days before illness. This model was the same for both variable selection algorithms used.

There was no significant difference between cases and controls in the degree to which they preferred their hamburgers cooked, the ability to recognize an adequately cooked hamburger or whether they would send back a hamburger that was not adequately cooked. When cases and controls are considered together, 63% stated they normally ate their hamburgers well done, although 9% of these people chose a picture of a medium cooked hamburger as the type they normally ate. Forty per cent of people who indicated that they prefer well done hamburgers, said they would eat a pink hamburger if served to them rather than ask that the hamburger be cooked longer.

DISCUSSION

This study provides further evidence of the importance of consuming undercooked hamburger in the transmission of *E coli* 0157:H7 infection. This finding is consistent with other case-control studies (14,15) as well as a number of outbreak investigations (3,17). *E coli* 0157:H7 is a well-documented inhabitant of the bovine gastrointestinal tract that has the po-

tential to contaminate beef carcasses at slaughter (18,19). In contrast to ground beef, other cuts of beef such as steaks were not associated with illness in this study. Hamburger may provide a better medium for the growth of this organism than solid cuts of meat because of its greater surface area and the spread of contamination throughout the product (19). Interestingly, no association was found between illness and consumption of other types of ground meat. This may reflect the lower rate of carriage of *E coli* 0157:H7 in domestic animals other than cattle and consequently the lower risk of carcass contamination in these species during slaughter (19).

To estimate the extent to which an inability to determine correctly the degree to which hamburgers are cooked constitutes a risk factor for *E coli* 0157:H7 infection, cases and controls were shown photographs of hamburgers cooked to varying degrees. This method proved useful in standardizing the interpretation of participants' responses. Misclassification of the degree of cooking was documented, but was no greater among cases than controls. Public awareness of the dangers of improperly cooked hamburger has likely increased since this study was done because of increased media attention following several outbreaks, including a major one in Washington State in 1993. News articles on verocytotoxigenic *E coli* including serotype 0157:H7 in the *New York Times* increased from two to five articles per year between 1982 and 1992 to 30 to 50 articles per year between 1993 and 1997 (20). The effect of increased media attention on peoples' knowledge and behaviour concerning ground beef consumption requires further study.

The importance of person-to-person transmission of this pathogen was highlighted in this study by the finding that contact with a nonhousehold member suffering from diarrheal illness constituted a significant risk for infection. Furthermore, contact with household members with diarrheal illness and attendance at daycare were also found to be associated with infection in the unvariable analysis. Person-to-person spread has been shown to be an important means of transmission of this infection in outbreaks as well as for sporadic

cases. In the 1993 Washington State outbreak, 10% of the 501 reported cases were secondary cases and 11% were considered to be either primary or secondary (3), while a large outbreak in the Canadian Northwest Territories occurred primarily as a result of person-to-person transmission (11). In a study of sporadic cases, *E coli* 0157:H7 was cultured from the stool of 13 symptomatic family members of 113 index cases (21). Excretion of *E coli* 0157:H7 continued for up to over 43 days after the onset date of illness, showing that vigilant attention to hygiene is needed when caring for an infected individual.

No association was observed between duration of illness and the use of antibiotics or antidiarrheal agents. These results should be interpreted with caution because this study was designed with the principal objective of identifying risk factors for infection, not determining the efficacy of potential therapeutic regimens.

As with most case-control studies of foodborne illness, this study is subject to a number of potential biases. The majority of cases in this investigation had bloody diarrhea; hence the risk factors for infection that were identified may differ from the risk factors for milder disease. The potential for recall bias exists; however, an effort was made to minimize this impact by excluding individuals with an onset date of illness more than 15 days before notification of the relevant health unit. Since this study was undertaken, a number of additional risk

factors for *E coli* 0157:H7 infection have been proposed, including consuming contaminated vegetables and drinking water, swimming in contaminated water and direct contact with cattle (5,6,8,9,18). These variables should be examined in future case-control studies.

CONCLUSIONS

This study underscores the importance of the consumption of undercooked ground beef and person-to-person spread in the transmission of *E coli* 0157:H7 infection in Canada. Control efforts should continue to focus on identifying and implementing strategies to reduce the prevalence of this organism at all levels of the food chain. Health care workers should remain vigilant in their efforts to educate the public (for example, through the media or special information campaigns) about the risks associated with consuming inadequately cooked ground beef and the importance of personal hygiene in the prevention of enteric illness.

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