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Risk factors for *Salmonella* Typhimurium DT104 and non-DT104 infection: a Canadian multi-provincial case-control study

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SUMMARY

To identify risk factors for sporadic *Salmonella* Typhimurium definitive phage-type 104 (DT104) and non-DT104 diarrhoeal illness in Canada, we conducted a matched case-control study between 1999 and 2000. Cases were matched 1:1 on age and province of residence. Multivariate analysis suggested that recent antibiotic use [odds ratio (OR) 5·2, 95% confidence interval (CI) 1·8–15·3], living on a livestock farm (OR 4·9, 95% CI 1·9–18·9), and recent travel outside Canada (OR 4·1, 95% CI 1·2–13·8) are independent risk factors for DT104 illness. Similar analyses suggested that recent travel outside North America is a sizable risk factor for non-DT104 illness (OR 66·8, 95% CI 6·7–665·3). No food exposure was a risk factor in either analysis. Educating health-care providers and the public about appropriate antibiotic use and antimicrobial resistance is important. Appropriate administration of antibiotics to livestock, particularly cattle, and hygienic measures such as handwashing after contact with farm animals may reduce risk. Travel represents an important and probably underestimated risk factor for sporadic illness with *S.* Typhimurium. Improved national surveillance and detailed investigation of travel-related illness are required.

INTRODUCTION

Salmonella enterica serovar Typhimurium (*S.* Typhimurium) is among the most prevalent human *Salmonella* serovars worldwide [1]. In the United States and Canada, *S.* Typhimurium accounted for 23 and 21% respectively, of all *Salmonella* isolates reported in 2000 [2, 3]. Individuals infected with *S.* Typhimurium

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generally experience mild gastrointestinal symptoms of diarrhoea and abdominal cramps and, occasionally, chills, fever, head and/or body ache. The illness usually resolves completely by 7 days. However, more severe illness may occur in up to 11% of all *S*. Typhimurium cases, with infants, the elderly and immunosuppressed individuals at highest risk [4]. Occasionally, acute salmonellosis may trigger complications such as reactive arthritis and Reiter's syndrome [5]. Antibiotic treatment is warranted for severe or extra-intestinal salmonellosis with recommended therapeutic agents including ciprofloxacin, azithromycin, ceftriaxone and cefotaxime [6].

In general, the number of infections frequently caused by antimicrobial-resistant enteric pathogens such as *Salmonella enterica* serovar Typhimurium definitive phage-type 104 (DT104) has risen over the past decade in many regions of the world [7, 8]. In Canada, the DT104 strain was first isolated in 1989. In 2000, out of the 1317 laboratory-confirmed human cases of *S*. Typhimurium reported, 479/1246 (38%) of the isolates phage-typed by the National Laboratory for Enteric Pathogens (NLEP) were DT104. Out of 467 DT104 strains tested for antimicrobial resistance, 412 (88%) strains were penta-resistant (ACSSuT) (ampicillin, chloramphenicol, streptomycin, sulphonamides, and tetracycline) [3]. Resistance to other antimicrobials (including trimethoprim–sulphamethoxazole and nalidixic acid) has also been demonstrated in Canada [9, 10] and reduced effectiveness of ciprofloxacin has been seen elsewhere in the world [11].

A variety of risk factors have been associated with *S*. Typhimurium DT104 infection. Foodborne outbreak investigations have implicated diverse food items including unpasteurized dairy products [12], pork sausages, chicken, meat paste [13], fresh apple cider [14] and sesame seed paste [15]. Contact with farm animals [16], pets [17], reptiles [18] and natural pet treats [19] have also been associated with infection. Other studies have shown previous antimicrobial treatment to be linked to an increased risk of developing resistant salmonellosis [20]. Given the increasing prevalence of multi-resistant *S*. Typhimurium DT104 infection in Canada, it is important to elucidate the epidemiological and microbiological characteristics of this pathogen in order to develop appropriate evidence-based prevention and control strategies. The goal of this study is to identify risk factors for the sporadic occurrence of diarrhoeal illness due to both DT104 and non-DT104 *S*. Typhimurium in Canada.

METHODS

Cases

This study was conducted in the provinces of Alberta, British Columbia, Ontario and Saskatchewan between 1 December 1999 and 30 November 2000. Eligible cases were individuals with diarrhoeal illness who had *S*. Typhimurium isolated from stool samples. Due to the large population in Ontario, every second eligible case was selected. Cases were excluded if their primary residence was outside the study province, the questionnaire was completed 30 days or more after onset of diarrhoea, or if they were identified as secondary cases arising from a single household. Cases that were unreachable by telephone after 15 attempts, unable to speak English or withheld consent to participate were also excluded.

Controls

Controls, matched 1:1 on cases' age and province of residence, were randomly selected from provincial Ministry of Health registered persons databases (RPDB) which includes nearly all residents eligible for provincial health insurance coverage [21]. Prospective controls were contacted by telephone within 7 days of the matched case interview and were excluded if they met any of the following criteria: their primary residence was outside the study province, they reported symptoms of diarrhoea or exposure to a household member with salmonellosis in the 4 weeks prior to interview, they were unable to communicate in English, or could not be reached by telephone after six attempts. If the initial control was excluded, the next eligible name on the client registry list was selected and the process repeated until a successful match was made or more than 7 days elapsed from the corresponding case interview.

Questionnaire

Cases and controls were interviewed by telephone using a pre-tested, standardized questionnaire adapted from similar, previously validated survey instruments [20, 22]. Each case and their matched control were questioned about potential exposures occurring during the 5 days (or 30 days for antibiotic exposure) preceding the case's symptom onset date. Adults replied on behalf of children. Data collected included demographics; health history including previous medication use; recent travel history; animal contact;

Table 1. *Demographic characteristics of the study population*

Characteristic	*S.* Typhimurium non-DT104 cases			*S.* Typhimurium DT104 cases		
Number of pairs	258			138		
Median age (range)	13 years (0–89 years)			19 years (0–91 years)		
Case-control pairs (%)						
Alberta	87 (34%)			38 (28%)		
British Columbia	42 (16%)			14 (10%)		
Ontario	122 (47%)			85 (62%)		
Saskatchewan	7 (3%)			1 (1%)		
	Cases	Controls	*P* value	Cases	Controls	*P* value
Female gender (%)	132 (51%)	155 (60%)	0·05	67 (49%)	81 (59%)	0·09
High school education or less* (%)	129 (51%)	89 (35%)	0·001	66 (49%)	54 (39%)	0·10

* Education of adult cases and controls or proxy respondents (for children).

consumption of raw fruits and vegetables, unpasteurized dairy products, raw or undercooked eggs and meats; meals eaten outside the home; drinking water source; food hygiene practices and day-care attendance.

Laboratory methods

All *S.* Typhimurium isolates collected during the study period were phage-typed and tested for antimicrobial susceptibility at the NLEP by the microtitre dilution method (Sensititre™, Trek Diagnostics, Westlake, OH, USA). National Committee on Clinical Laboratory Standards (NCCLS) protocols were followed and break-points for antimicrobial agents were determined using current NCCLS interpretive standards (M100/S9, January 1999 and M31A, June 1999). Minimum inhibitory concentrations (MIC) were categorized as resistant, sensitive or intermediate, with intermediate results reclassified as sensitive. Appropriate quality control procedures were followed as per NCCLS standard protocols (M100-S9 and M7-A5) and the manufacturer's instructions.

Data management and analysis

Data were entered into Epi-Info version 6.04 (Centers for Disease Control and Prevention, Atlanta, GA, USA), verified by double entry and analysed using SPSS version 10.0 (SPSS Inc., Chicago, IL, USA). Matched bivariate analyses were performed for each potential risk factor using McNemar's test for dichotomous variables and paired *t* tests for continuous variables. Results are presented for factors with $P \leqslant 0{\cdot}05$ and factors with $P \leqslant 0{\cdot}25$ were included in the initial conditional logistic regression models. Variables with $P \leqslant 0{\cdot}05$ and gender, a potential confounder, were retained in the final models.

RESULTS

Case and control groups

During the 12-month study period, 640 case-patients with *S.* Typhimurium infection were identified. Of the 577 case-patients reached by telephone, 20 did not speak English, 22 declined to participate and 112 did not fulfil the inclusion criteria. A further 29 study cases were excluded because an appropriate matched control was not found in time. There were no known outbreak-associated cases. Ultimately, 138 case-control pairs met the criteria for the *S.* Typhimurium DT104 risk-factor analyses and 258 pairs for the *S.* Typhimurium non-DT104 analyses (Table 1). Fifty-two phage-types comprised the non-DT104 group, predominantly phage-types 208 (20%) and 124 (16%).

DT104 and non-DT104 cases were similar with respect to median age ($P = 0{\cdot}06$, median test) and gender distribution. Overall, the majority of cases resided in the province of Ontario (62% of the DT104 cases and 47% of the non-DT104 cases). Compared to their matched controls, non-DT104 cases differed ($P \leqslant 0{\cdot}05$) by both gender and reported level of formal education; these differences were not statistically significant in the DT104 case-control group. Educational level referred to that of adult cases and controls or proxy respondents for either cases or controls.

Table 2. *Matched pair bivariable analysis for non-food exposures:* S. *Typhimurium DT104 and non-DT104 infection, Canada, 1999–2000*

	S. Typhimurium non-DT104			*S.* Typhimurium DT104		
Variable	OR	95% CI	*P* value	OR	95% CI	*P* value
Antibiotics taken in 4 weeks prior to illness	1·3	0·6–3·2	0·56	3·7	1·4–10·1	0·004
Anti-diarrhoeal medication in 4 weeks prior to illness	8·0	1·0–170·6	0·04	1·3	0·2–7·5	1·00
Chronic disease†	1·9	1·1–3·2	0·02	2·2	0·9–5·3	0·06
Any travel in last 5 days	1·8	1·2–2·8	0·01	1·5	0·8–2·9	0·27
Travel outside Canada and USA in past 5 days	20·0	2·9–400·5	<0·001	—‡	2·1–∞	0·003
Been on a livestock farm in past 5 days	1·7	0·9–2·9	0·08	2·4	1·0–5·9	0·05
Live on a livestock farm	2·4	1·1–5·7	0·03	4·3	1·2–19·1	0·02
Contact with cattle	1·4	0·6–2·8	0·49	4·3	1·2–19·1	0·02
Contact with a pet bird	0·4	0·2–1·0	0·04	0·9	0·3–2·5	1·00
Municipal drinking water	0·6	0·4–1·0	0·03	0·8	0·4–1·5	0·66

† For example, asthma, allergies, heart disease, arthritis, musculoskeletal disease, diabetes.
‡ Undefined.

Matched bivariable analysis

For both DT104 and non-DT104 groups, recent travel was strongly associated with increased risk of illness (Table 2). Being on a livestock farm in the 5 days before onset of illness was associated with increased risk in the DT104 group, but the evidence was less clear for the non-DT104 group. For the non-DT104 group, additional risk factors included taking anti-diarrhoeal medication in the 4 weeks before illness and having a pre-existing chronic disease that was not gastrointestinal in nature (e.g. asthma, allergies, heart disease, arthritis, musculoskeletal disease, diabetes).

Overall, taking antibiotics in the 4 weeks before illness was associated with illness in the DT104 group, but not in the non-DT104 group. A preliminary analysis (results not shown) suggested that resistance patterns differed for Ontario, so we tested whether prior antibiotic use differed spatially. DT104 cases in Ontario were more likely to report prior antibiotic use (OR 2·2, CI 0·7–7·3) whereas non-DT104 cases were less likely to report it (OR 0·14, CI 0·01–1·14), but both results were non-significant. In the other provinces, prior antibiotic use was associated with illness for both DT104 (OR 11·0, CI 1·5–228·1) and non-DT104 groups (OR 3·5, CI 1·1–12·6).

Overall, 23/138 (17%) DT104 cases took antibiotics in the 4 weeks prior to illness. Of the 20 cases that recalled the antibiotics taken, 15 (75%) had taken antibiotics to which their *S.* Typhimurium isolate was resistant. For non-DT104 cases, 18/258 (7%) took antibiotics in the 4 weeks prior to illness. Of the 14 cases that provided the names of the antibiotics, 9 (64%) had taken antibiotics to which their *S.* Typhimurium isolate was resistant.

Non-DT104 cases were more likely than their controls to have consumed chicken prepared outside the home (Table 3). All other significant food and kitchen hygiene exposures associated with DT104 and non-DT104 illness were inversely associated with illness.

Multivariable analysis using conditional logistic regression modelling

Travel outside Canada was an independent risk factor for DT104 illness (Table 4). Cases that travelled had been to Cuba (5/14), the United States (3/14), Mexico (2/14), Portugal (2/14), and Belgium, Holland, and Syria (1/14 each) whereas controls that travelled outside Canada had only been to the United States (6/6) in the past 5 days. Travel outside Canada and the United States was independently and strongly associated with non-DT104 illness and included trips by cases to Mexico (11/20), Southeast Asia/China (4/20), Cuba (2/20), other Caribbean countries (3/20), and Portugal (1/20).

Taking antibiotics in the previous 4 weeks remained a significant and independent risk factor for DT104

Table 3. *Matched pair bivariable analysis for food and kitchen hygiene exposures:* S. *Typhimurium DT104 and non-DT104 infection, Canada, 1999–2000*

	S. Typhimurium non-DT104			*S.* Typhimurium DT104		
Variable	OR	95% CI	*P* value	OR	95% CI	*P* value
Food brought from home to work/school	0·6	0·4–0·9	0·005	0·9	0·5–1·7	1·00
Ate green salad	0·4	0·3–0·7	<0·001	0·5	0·3–0·9	0·01
Consumed fresh fruit juice (unpasteurized)	0·5	0·3–0·8	0·01	0·5	0·2–1·2	0·15
Ate scrambled eggs, omelette	0·7	0·5–1·0	0·05	0·5	0·3–0·9	0·01
Ate other type of eggs (e.g. boiled)	0·5	0·3–0·7	<0·001	0·5	0·2–1·2	0·15
Ate hamburger patties	0·6	0·4–0·9	0·01	0·9	0·5–1·5	0·79
Ate meals made at home containing hamburger	0·1	0·01–1·0	0·05	1·2	0·3–4·5	1·00
Ate beef (other than hamburgers)	0·5	0·4–0·8	0·001	0·8	0·5–1·4	0·55
Ate pork	0·5	0·3–0·7	<0·001	0·6	0·3–1·2	0·16
Ate delicatessen meats in past 5 days	0·6	0·4–0·9	0·004	0·7	0·4–1·2	0·20
Ate hot dogs	0·6	0·4–0·9	0·01	0·91	0·5–1·5	0·80
Ate chicken	0·6	0·4–1·0	0·07	0·5	0·2–0·9	0·01
Ate chicken outside of home	2·8	1·6–4·9	<0·001	1·8	0·9–3·8	0·10
Touched raw meat	0·6	0·3–0·9	0·01	0·4	0·2–0·8	0·01

Table 4. *Final conditional logistic regression models for risk exposures:* S. *Typhimurium DT104 and non-DT104 infection, Canada, 1999–2000*

	S. Typhimurium non-DT104 ($n=194$)			*S.* Typhimurium DT104 ($n=123$)		
Variable	OR	95% CI	*P* value	OR	95% CI	*P* value
Antibiotics taken in 4 weeks before illness		*		5·2	1·8–15·3	0·002
Live on a livestock farm		†		4·9	1·3–18·9	0·02
Travel outside Canada and USA	66·8	6·7–665·3	<0·001		‡	
Travel outside Canada		§		4·1	1·2–13·8	0·02
Ate green salad	0·4	0·2–0·7	0·001	0·5	0·3–1·0	0·05
Consumed fresh fruit juice	0·3	0·2–0·7	0·01		*	
Ate chicken		†		0·5	0·2–1·0	0·05
Ate pork (chops, roast, etc.)	0·4	0·2–0·6	<0·001		*	
Sex (F=1, M=0)	0·5	0·3–0·8	0·01	0·7	0·4–1·2	0·18
High school education or less *vs.* more than high school education	0·6	0·3–0·9	0·03		*	

* Not offered to initial multivariate model.
† Not retained in final model.
‡ Estimates could not be computed because of a zero cell (i.e. 11 cases and 0 matched controls travelled outside Canada and the United States in the 5 days before illness).
§ Not computed.

illness. Also consistent with the bivariate analysis, in British Columbia, Alberta and Saskatchewan combined, prior antibiotic use was associated (OR 10·9, 95% CI 1·3–90·8) with DT104 illness. DT104 cases in Ontario were more likely to report prior antibiotic use (OR 3·2, 95% CI 0·9–11·0), but this result was not statistically significant.

Living on a livestock farm was significantly associated with DT104 illness after controlling for other factors, but was not a risk factor for non-DT104 infection.

Eating green salad or chicken was associated with lower risk of illness in the DT104 group, whereas drinking fresh fruit juice, eating green salad or eating

pork was associated with lower risk of non-DT104 illness.

DISCUSSION

The results of this study show that previous antibiotic use, living on a livestock farm and recent international travel are risk factors for DT104 illness whereas travel outside of Canada and the United States significantly increases the risk of non-DT104 illness.

Previous antibiotic use

Our study showed that people infected with *S*. Typhimurium DT104 were five times more likely to have been on antibiotics in the 4 weeks prior to becoming ill compared to controls for the same time period. This finding is in accord with a US case-control study which found cases with multi-resistant DT104 infection three times more likely to have taken antibiotics in the 4 weeks before onset of illness than controls [20]. Similarly, a French study of sporadic *S*. Typhimurium illness in children showed cases were more than twice as likely as their matched controls to have taken antibiotics in the month before onset of illness [23].

Previous antimicrobial use was a significant risk factor for *S*. Typhimurium DT104 in three of the four participating provinces. These three provinces are contiguous and situated in western Canada. It is possible that antimicrobial use (e.g. prescribing patterns) differs geographically, that the prevalence of *S*. Typhimurium strains differ geographically, and that residents of western Canada travel to different destinations than Ontario residents. These factors may contribute to regional variations.

Prior antimicrobial use may increase susceptibility to ingested *Salmonella* through several mechanisms, including selective pressure which would preferentially support the growth of resistant organisms or alterations of the gut flora which would favour the proliferation of both resistant and sensitive strains. It is also possible that sub-clinical DT104 infection already exists and antibiotic use, might be sufficient to induce a clinical case of DT104 [24].

Given the mounting evidence implicating prior antimicrobial use as a risk factor for human *S*. Typhimurium illness, it is important to educate health-care providers and the public about appropriate antibiotic use and the potential for developing a resistant infection in the future.

Farm

We found that people infected with *S*. Typhimurium DT104 were over four times more likely to live on a livestock farm than controls. In our study, contact with cattle was the most likely exposure on the farm, with half of the cases residing on farms reporting close/touching contact with cattle. Additional, indirect exposures could include dispersed cattle and pig manure [25] and contaminated feeds or fertilizers [26].

Previous epidemiological studies have shown that contact with cattle contributes to both direct and indirect transmission of zoonotic pathogens such as *S*. Typhimurium DT104 [16, 27] and verocytotoxigenic *E. coli* [28]. In Canada, 49% of bovine isolates submitted to Health Canada's Laboratory for Foodborne Zoonoses for routine testing were *S*. Typhimurium or *S*. Typhimurium var. Copenhagen and 33 and 60% respectively, were phage-type 104 [29]. In Prince Edward Island, Canada, salmonellae were isolated from 4·6% of beef cattle sampled at slaughter. Of the isolates, 64% were *S*. Typhimurium phage-type 104 [30].

These findings underscore the importance of primary prevention of infection of livestock and measures to reduce direct and indirect zoonotic spread to humans. Given that cattle and other livestock can serve as a reservoir for *S*. Typhimurium, the institution of on-farm food safety programmes that include prudent use of antimicrobials and management of manure and farm run-off is important. Hygienic measures, particularly handwashing after contact with farm animals, may also help control transmission to farmers and their families [31].

Travel

The results of this study consistently suggest that recent travel outside Canada is associated with increased risk of *S*. Typhimurium. The importance of travel as a risk factor for infection with *S*. Typhimurium has not been well quantified in the literature. Some case-control studies have excluded travellers [13, 32] whereas others have not reported a significant association with travel [20, 23]. However, recent travel abroad was a sizable risk factor for non-enteritidis salmonellae cases in a study of sporadic salmonellosis in Switzerland [33]. Kapperud et al. [34] found foreign travel among household members of cases in Norway to be an independent risk factor for *S*. Typhimurium infection.

It is plausible that individuals who have recently travelled are more likely to seek medical attention and that physicians are more likely to request stool samples if they know that their patients have travelled recently. Given that 8% of *S.* Typhimurium cases in this study thought they may have become ill as a result of travel, this is reasonable. Since *S.* Typhimurium is common in many countries, including those with tropical and sub-tropical climates that are popular tourist destinations for Canadians [35], and only a fraction of travellers with gastroenteritis are identified through routine public-health surveillance [36], travel represents an important and probably underestimated risk factor for sporadic illness with *S.* Typhimurium in Canada. Our findings support the need for appropriate interventions aimed at Canadian travellers and their physicians, including evidence-based preventive strategies and treatment recommendations. These results emphasize recommendations by Canada's Committee to Advise on Tropical Medicine and Travel that we be more judicious as antimicrobially resistant organisms become more prevalent and that chemoprophylaxis for travellers' diarrhoea should be restricted to high-risk, short-term travellers [37].

Improved national surveillance and more detailed investigation of travel-related illness are required to more accurately assess the magnitude, impact and sources of travel-related gastroenteritis.

Foods

Outbreak investigations of both *S.* Typhimurium DT104 and non-DT104 infections have implicated a wide variety of foods including beef, turkey, salad vegetables, and raw ground beef. However, recently published case-control studies of sporadic infections found mixed associations with foods in multivariate analysis [13, 20, 23, 34]. In our study we found that several foods, which had been linked to published outbreaks, were inversely associated with sporadic illness. It is possible that consumption of certain of these foods (e.g. green salad or fresh fruit juice) may be protective, through as yet speculative mechanisms, or they may be indicators of nutritional status and possibly be related to better health in general. It is also possible that the time lag between exposure period and interview (up to 30 days for cases and 37 days for controls) and the lack of a recall stimulus for controls influenced our findings. Particularly when there are sizable time delays between disease onset and data collection in studies of sporadic enteric illness, cases' responses regarding food exposures may reflect common conceptions about causes of foodborne illness rather than actual behaviours whereas controls are likely to report what they usually eat [38–40]. Given that no microbiological testing of food exposures was conducted, cross-contamination may also obscure risk-factor results [41].

Limitations

The effects of potential recall inaccuracy and bias need to be considered in case-control studies of sporadic enteric illness, particularly for food exposures. In our study, we attempted to reduce recall inaccuracy by interviewing cases within 30 days of onset of illness and controls within 7 days of the matched case, but this may not have been prompt enough for accurate and unbiased recall. Measures to reduce time lags at all steps in the enteric disease reporting chain and particularly between onset of illness and interview would optimize case-control study effectiveness for sporadic gastrointestinal illness. Questionnaires for sporadic enteric illness have been designed that incorporate several exposure windows (e.g. 3 days and 1 week) [42] that may aid in detecting food risk factors, particularly when foods are common. In our study, potential controls were excluded if they could not be reached by telephone after six attempts. This differed from cases that were excluded after 15 attempts and this differential follow-up may have affected study results. Whereas interviewers were unaware of the phage-type and resistance profile of the cases' infections at the time of the interview, interviewers were not blinded to the case-control status of respondents. However, comprehensive interviewer training materials and standardized case and control survey instruments were used to minimize potential information bias.

CONCLUSIONS

Our study identified travel outside Canada as a risk factor for sporadic *S.* Typhimurium illness. Previous antibiotic use and living on a livestock farm were risk factors for sporadic *S.* Typhimurium DT104 illness in particular. Therefore, public health, veterinary and medical professionals should promote activities associated with these specific risk factors that reduce the risk of contracting this illness.

APPENDIX. The Multi-Provincial *Salmonella* Typhimurium Case-Control Study Steering Committee

Murray Fyfe, Jane Buxton, Arlene King and Ana Paccagnella (British Columbia Centre for Disease Control); Karen Grimsrud (Alberta Health & Wellness); Ingrid Zazulak (Capital Health, Edmonton); James Talbot and Robert Rennie (Provincial Laboratory of Public Health for Northern Alberta); Peter Pieroni (Laboratory & Disease Control Services Branch, Saskatchewan Health); Rafiq Ahmed and Frank Rodgers (National Laboratory for Enteric Pathogens, Health Canada); Franklin Pollari, Kathryn Doré and Jeffrey Wilson (Foodborne, Waterborne and Zoonotic Infections Division, Health Canada); Pascal Michel (Laboratory for Foodborne Zoonoses, Health Canada); Dean Middleton, Monika Naus, Bonnie Henry, Bruce Cieben and Frances Jamieson (Ontario Ministry of Health & Long Term Care).

REFERENCES

1. Gomez TM, Motarjemi Y, Miyagawa S, Kaferstein FK, Stohr K. Foodborne salmonellosis. World Health Stat Q 1997; **50**: 81–89.
2. Centers for Disease Control and Prevention. National Antimicrobial Resistance Monitoring System (NARMS) Surveillance Report: 2000. Atlanta: Centers for Disease Control and Prevention, 2001.
3. Demczuk W, Ahmed R, Woodward D, Clark C, Rodgers F. Laboratory surveillance data for enteric pathogens in Canada: 2000 annual summary. Health Canada, 2001.
4. Honish L. Restaurant-associated outbreak of *Salmonella typhimurium* phage type 1 gastroenteritis – Edmonton, 1999. Can Commun Dis Rep 2000; **26**: 25–28.
5. Threlfall EJ, Ward LR, Rowe B. Multiresistant *Salmonella typhimurium* DT104 and salmonella bacteraemia. Lancet 1998; **352**: 287–288.
6. Bartlett JG. Pocket book of infectious disease therapy. Philadelphia: Lippincott, Williams and Wilkins, 2000.
7. Marano N, Rossiter S, Stamey K, et al. The National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria, 1996–1999: surveillance for action. J Am Vet Med Assoc 2000; **217**: 1829–1830.
8. Poppe C, Smart N, Khakhria R, Johnson W, Spika J, Prescott J. *Salmonella typhimurium* DT104: a virulent and drug-resistant pathogen. Can Vet J 1998; **39**: 559–565.
9. Khakhria R, Mulvey M, Ahmed R, Woodward D, Johnson W. Emergence of multi-resistant strain of *Salmonella* Typhimurium phage type 104 (DT104) in Canada [poster P22-19]. In: Program and abstracts, International Conference on Emerging Infectious Diseases, 8–11 March 1998 (Atlanta), p. 141.
10. Harnett N, Wan J, Brunins V, Borczyk A, Khakhria R, Johnson W. Human isolates of *Salmonella typhimurium* DT104 in Ontario. Can Commun Dis Rep 1998; **24**: 20–23.
11. Mølbak K, Baggesen DL, Aarestrup FM, et al. An outbreak of multidrug-resistant, quinolone-resistant *Salmonella enterica* serotype Typhimurium DT104. New Engl J Med 1999; **341**: 1420–1425.
12. Cody SH. Multidrug-resistant *Salmonella* outbreaks linked to raw-milk products. JAMA 1999; **281**: 1845–1847.
13. Wall PG, Morgan D, Lamden L, et al. A case-control study of infection with an epidemic strain of multiresistant *Salmonella typhimurium* DT104 in England and Wales. Commun Dis Rep CDR Rev 1994; **4**: R130–R135.
14. Centers for Disease Control and Prevention. Epidemiological notes and reports: *Salmonella typhimurium* outbreak traced to a commercial apple cider – New Jersey. MMWR 1975; **24**: 87–88.
15. Brockmann S. International outbreak of *Salmonella* Typhimurium DT104 due to contaminated sesame seed products – update from Germany (Baden-Württemberg). Eurosurveillance Weekly 2001; 16 Aug., 5.
16. Besser TE, Gay CC, Gay JM, et al. *Salmonella* associated with *S. typhimurium* DT 104 in the USA. Vet Rec 1997; **140**: 75.
17. Wall PG, Threlfall EJ, Ward LR, Rowe B. Multiresistant *Salmonella typhimurium* DT104 in cats: a public health risk. Lancet 1996; **348**: 471.
18. Centers for Disease Control and Prevention. Reptile-associated salmonellosis – selected states, 1996–1998. MMWR 1999; **48**: 1009–1013.
19. Laboratory Centre for Disease Control, Health Canada. Human health risk from exposure to natural dog treats. Can Commun Dis Rep 2000; 26-06: 41–42.
20. Glynn MK, Reddy S, Fiorentino T, et al. Antimicrobial agent use increases infections with resistant bacteria: a FoodNet case-control study of sporadic, multiresistant *Salmonella typhimurium* DT 104 infections, 1996–1997. Program and abstracts of the 36th Annual Meeting of the Infectious Diseases Society of America, 1998; 12–15 November; Denver, CO. Alexandria, VA: Infectious Diseases Society of America, 1998: 84 [abstract 52].
21. Krenten-Boaretto B, Buxton JA, Doré K, Fyfe M, Middleton D, McEwen S, and the Multi-Provincial *Salmonella* Typhimurium Case-Control Study Group. Using Provincial Client Registries for Control Selection; Lessons Learned. Canada Communicable Disease Report. 2003, 29-20: 173–179.
22. PHLS study of infections with multidrug resistant *Salmonella typhimurium* DT104 has recruited enough cases (Editorial). Commun Dis Rep CDR Wkly 1998; **8**: 123.
23. Delarocque-Astagneau E, Bouillant C, Vaillant V, Bouvet P, Grimont P, Desenclos J-C. Risk factors for the occurrence of sporadic *Salmonella enterica* serotype

typhimurium infections in children in France: a national case-control study. Clin Inf Dis 2000; **31**: 488–492.
24. Cohen ML, Tauxe RV. Drug-resistant *Salmonella* in the United States: an epidemiological perspective. Science 1986; **234**: 964–969.
25. VanPelt W. Explosive increase in multiresistant *Salmonella* Typhimurium DT104 in 2001 in the Netherlands. Eurosurveillance Weekly, 2001, 13 Dec., 5.
26. Chin J, ed. Control of communicable diseases manual. 17th edn. 2000. Washington: American Public Health Association, 2000.
27. Fone DL, Barker RM. Associations between human and farm animal infections with *Salmonella typhimurium* DT104 in Herefordshire. Commun Dis Rep CDR Rev 1994; **4**: R136–R140.
28. Michel P, Wilson JB, Martin SW, Clake RC, McEwen SA, Gyles CL. Temporal and geographical distributions of reported cases of *Escherichia coli* O157:H7 infection in Ontario. Epidemiol Infect 1999; **122**: 193–200.
29. Cole LM, Muckle CA, Poppe C. *Salmonella* serovars and *Salmonella* phagetypes identified by the O.I.E. reference laboratory for salmonellosis at the health canada laboratory for foodborne zoonoses. Year 2000 annual report. Guelph (Ontario): Health Canada Laboratory for Foodborne Zoonoses, 2001.
30. Abouzeed YM, Hariharan H, Poppe C, Kibenge FS. Characterization of *Salmonella* isolates from beef cattle, broiler chickens and human sources on Prince Edward Island. Comp Immunol Microbiol Infect Dis 2000; **23**: 253–266.
31. Friedman CR, Torigian C, Shillam PJ, et al. An outbreak of salmonellosis among children attending a reptile exhibit at a zoo. J Pediatr 1998; **132**: 802–807.
32. Wall PG, Morgan D, Lamden K, et al. Transmission of multi-resistant strains of *Salmonella typhimurium* from cattle to man. Vet Rec 1995; **136**: 591–592.
33. Schmid H, Burnens AP, Baumgartner A, Oberreich J. Risk factors for sporadic salmonellosis in Switzerland. Eur J Clin Microbiol Infect Dis 1996; **15**: 725–732.
34. Kapperud G, Lassen J, Hasseltvedt V. *Salmonella* infections in Norway: descriptive epidemiology and a case-control study. Epidemiol Infect 1998; **121**: 569–577.
35. Gutierrez-Cogco L, Montiel-Vazquez E, Aguilera-Perez P, Gonzalez-Andrade MC. *Salmonella* serotypes identified in Mexican health services [in Spanish]. Salud Publica Mex 2000; **42**: 490–495.
36. Division of Enteric, Foodborne and Waterborne Diseases, Centre for Infectious Disease Prevention and Control and the National Laboratory for Enteric Pathogens, Bureau of Microbiology, Population and Public Health Branch, Health Canada. Risk of enteric illness associated with travel: a case review of gastroenteritis among Canadian travellers: January to April, 2000. Can Commun Dis Rep 2001; **27**: 45–49.
37. Committee to Advise on Tropical Medicine and Travel (CATMAT). Statement on travellers' diarrhoea. Can Commun Dis Rep 2001; **27** (ACS-3): 1–12.
38. Rothman KJ, Greenland S. In: Modern epidemiology, 2nd edn. Philadelphia: Lippincott Williams & Wilkins, 1998.
39. Klemetti A, Saxen L. Prospective versus retrospective approach in the search for environmental causes of malformations. Am J Public Health 1967; **57**: 2071–2075.
40. Coughlin SS. Recall bias in epidemiological studies. J Clin Epidemiol 1990; **43**: 87–91.
41. Palmer SR. A review: epidemiological methods in the investigation of food poisoning outbreaks. Lett Appl Microbiol 1990; **11**: 109–115.
42. Cowden JM, Lynch D, Joseph CA, et al. Case-control study of infections with *Salmonella enteritidis* phage type 4 in England. BMJ 1989; **299**: 771–773.