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Point source outbreaks of *Campylobacter jejuni* infection – are they more common than we think and what might cause them?

THE *CAMPYLOBACTER* SENTINEL SURVEILLANCE SCHEME COLLABORATORS*

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SUMMARY

Despite being the commonest bacterial cause of infectious intestinal disease (IID) in England and Wales, outbreaks of campylobacter infection are rarely reported. However, data from the *Campylobacter* Sentinel Surveillance Scheme suggested that outbreaks might be more common than was previously suspected, since a high proportion of cases reported other illness in the home or in the community at the same time as their illness. To identify factors that might lead to these apparent outbreaks, the exposures of cases of *Campylobacter jejuni* infection reporting other illness, either in the home or the community, were compared with those for cases not reporting other illness using case–case methodology. Illness in the home was associated with consuming organic meats in the winter, having contact with a pet suffering from diarrhoea or visiting a farm in the 2 weeks before the onset of symptoms. Illness in the community was associated with the consumption of foods in restaurants or drinking unpasteurized milk. Prevention of campylobacter infection requires that better methods of outbreak detection and investigation are developed, which in turn should lead to a better understanding of risk factors.

INTRODUCTION

Campylobacters are the commonest bacterial cause of infectious intestinal disease (IID) in England and Wales [1]. Laboratory reports of faecal isolates have exceeded 50 000 cases annually for the past 5 years [1], and these cases represent a fraction of those cases thought to occur in the community at large [2]. Despite this, outbreaks of campylobacter infection are rarely reported, with only 2% of all outbreaks of IID reported to the Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre (CDSC) between 1992 and 1999 being attributed to this pathogen [3, 4].

Outbreaks of campylobacter infection might go unrecognized for several reasons. Firstly, the long incubation period [5] means that cases might not recall

certain common exposures, or that exposure might have occurred outside the period of enquiry. Secondly, investigators might have insufficient resources to investigate such large numbers of individual cases [6]. Finally, having identified a cluster of cases in space and time, investigators have not, until relatively recently, had a central reference facility to add microbiological typing evidence to epidemiological information, which is often needed in the recognition or confirmation of outbreaks [4].

The epidemiological and microbiological evidence gained from outbreak investigations provides valuable data on the sources and vehicles of infection [7]. The lack of recognized outbreaks means that risk factors for campylobacter infection are not easily identified, and this hampers the identification, implementation and monitoring of intervention strategies.

The *Campylobacter* Sentinel Surveillance Scheme, which was launched in May 2000, aims to generate new hypotheses for campylobacter infection through

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the integration of standardized epidemiological and microbiological typing data [8]. Data from the first year of the scheme suggested that point source outbreaks of campylobacter infection might be more common than was previously suspected, with a high proportion of cases reporting concurrent illness in the home or in the community [9, 10].

The aim of this study was to determine what factors, if any, might lead to these apparent outbreaks, by comparing the exposures of cases reporting other illness, either in the home or the community, with those cases who did not, using case–case methodology [11].

METHODS

Epidemiological information for all laboratory-confirmed campylobacter cases in the participating health authorities was collected using a standard, structured questionnaire. Demographic and clinical information was captured, in addition to the patients' travel history and exposures to food, water, the environment and animals in the 2 weeks prior to illness. Completed questionnaires were forwarded to the Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre (CDSC) for data entry. Laboratory isolates were referred to the *Campylobacter* Reference Unit of the PHLS Laboratory of Enteric Pathogens for speciation [12], serotyping [13], phage typing [14] and antimicrobial resistance testing [15].

The epidemiological and typing datasets were combined using the patients' surnames and dates of birth, and analysed using Stata version seven (Stata Corporation, College Station, TX, USA). The date of onset was used to define the season in which illness commenced. 'Spring' was defined as March to May, 'summer' from June to August, 'autumn' from September to November and 'winter' from December to February. Standard occupational classification was employed to determine cases' socio-economic group [16]. Additional categories were created for individuals who described their occupation as unemployed, pre-school child, school child, student, homemaker, retired, part time, and for those who were unable to work due to disabilities or long-term illness. Food exposures were coded to compare those who had eaten a particular food in the 2 weeks prior to onset (once or more than once) with those who had not. Contact with raw meat was coded to compare no contact with 1, 2–5, 6–10 and more than 11 times. Daily water

consumption was coded to differentiate no exposure from 1 to 4, 5 to 9 and 10 or more glasses of water drunk.

Patient age was stratified into 10-year age groups. Household size was recorded to compare those households with 1–4 (adults or children), with 5–9 and with 10 or more members. Individuals with missing data were omitted from the analyses using those data items.

For the case–case comparison, cases of *C. jejuni* infection who reported individuals with similar symptoms at the same time (either in their home or in the community) were considered 'cases'. The epidemiological data for these 'cases' were scrutinized, and where other individual or individuals were infected with a different pathogen (confirmed, other than campylobacter), or where the onset of illness was greater than 7 days from that of the 'case', that 'case' was excluded. 'Controls' were those cases of *C. jejuni* infection who did not report other illness in either the home or the community. For the analysis of household illness, all cases who reported living alone were excluded from the analysis.

Demographic and clinical differences were assessed using Pearson's χ^2 test and the Student's *t* test. Initial comparisons were undertaken using single risk variable analyses. Mantel–Haenszel odds ratios (OR) were calculated for each explanatory variable. Logistic regression was then applied to obtain maximum-likelihood estimates of the effect of exposures on the outcome of interest whilst controlling for confounding. Variables with a $P < 0.1$ from the single risk variable analysis were included initially and the model was simplified using the likelihood ratio (LR) test. Potential interactions (between the main effects included in the initial logistic regression model and age, gender and season) were also examined using this method.

RESULTS

Linked data were available for 3489 cases of *C. jejuni* infection reported during the first year of the surveillance scheme. Cases ranged from less than 1 month to 94 years in age (mean 39) and the gender distribution was even. Diarrhoea (96%), abdominal pain (86%) and fever (81%) were the most commonly reported symptoms, and over a quarter (28%) of cases reported bloody diarrhoea. Cases amassed 37386 days of illness (range 0–701 days) and 358 cases (10%) were admitted to hospital for at least 1400 days.

Table 1. Risk exposures for illness in the home – single risk variable analysis (exposures with a $P < 0.1$ are shown)

Exposure	Percent exposed		OR*	P	95% CI†	
	'Cases'	'Controls'			Lower	Upper
Increasing 10 year age group	—	—	0.85	<0.001	0.81	0.89
Skilled manual workers	3.7	6.7	0.53	0.02	0.32	0.90
Unemployed workers	0.5	1.8	0.25	0.04	0.06	1.04
School children	10.4	4.9	2.28	<0.001	1.59	3.28
Pre-school children	20.0	8.0	2.86	<0.001	2.16	3.79
British ethnicity	82.5	88.6	0.61	<0.001	0.45	0.82
Asian ethnicity	10.5	5.6	1.98	<0.001	1.36	2.89
Travel abroad	26.6	18.5	1.59	<0.001	1.26	2.00
Baby food	8.9	4.2	2.26	<0.001	1.48	3.44
Barbecued food	22.1	18.4	1.26	0.08	0.97	1.62
Beef (incl. roast, mince, steak)	68.6	72.5	0.82	0.09	0.83	0.10
Cold meats (pre-cooked)	63.5	73.9	0.61	<0.001	0.49	0.77
Halal meats	9.4	7.0	1.39	0.08	0.96	2.00
Organic meats	6.0	3.9	1.56	0.06	0.98	2.50
Pork, ham or bacon	74.5	80.7	0.70	0.003	0.55	0.89
Pre-packed sandwiches	33.8	44.4	0.64	<0.001	0.51	0.80
Handling raw meat (increasing frequency)	—	—	0.83	<0.001	0.76	0.91
Unpasteurized milk	10.7	7.6	1.45	0.03	1.03	2.04
Engineering work or supply problems (water)	9.7	5.0	2.07	<0.001	1.43	2.98
Swimming	28.6	19.2	1.69	<0.001	1.35	2.12
Sailing	3.88	1.66	2.39	0.002	1.34	4.28
Contact with a pet horse	2.2	1.0	2.18	0.04	1.00	4.74
Contact with a pet rodent	7.5	4.4	1.76	0.008	1.15	2.69
Contact with a pet with diarrhoea	11.8	6.5	1.93	0.005	1.21	3.10
Visiting a farm	15.9	9.6	1.79	0.001	1.25	2.55
Increasing number of household members	—	—	1.08	<0.001	1.03	1.13

* Odds ratio; † exact confidence interval.

Other illness in the household

Of the 3070 cases of *C. jejuni* infection who did not live alone, 509 cases (17%) reported another individual or individuals within the household with similar symptoms at the same time (66 cases did not respond to the question). Of the 509 cases reporting other persons with similar illness, 41 cases reported that the other ill individual or individuals had a date of onset greater than 1 week from the case and three individuals were confirmed as being infected with another gastrointestinal pathogen. These cases were excluded, leaving 465 'cases' and 2495 'controls'.

Cases tended to be younger (mean age 30.2 years) than controls (mean age 37.5) (t test, $P < 0.001$) and were more likely to report vomiting (44.7 vs. 39.4%; $P = 0.04$) and abdominal pain (94.5 vs. 92.0%; $P = 0.04$). There were no differences in gender (51.6 vs. 50.5% male), length of illness (11.4 days each) or admission to hospital (9.5 vs. 10.5%).

Exposures in the fortnight prior to illness (Single risk variable analysis)

Cases were more likely to be school children or pre-school children than controls and were more likely to be Asian (Table 1). They were more likely to have travelled outside the United Kingdom in the 2 weeks before illness and to report the consumption of certain foods, engineering work or problems with their water supply, or recreational exposure to water. They were more likely to have had contact with certain animals, or to have visited a farm in the 2 weeks prior to the onset of symptoms.

Independent exposures in the fortnight prior to illness (logistic regression analysis)

Cases were more likely to be pre-school or school children than controls (Table 2). They were more likely to have consumed organic meats in the winter, to have had contact with a pet suffering from

Table 2. Independent risk exposures for illness in the home (logistic regression model controlling for age and gender)

Exposure	OR*	P	95% CI†	
			Lower	Upper
Organic meats in the winter	6.86	0.014	1.49	31.69
School children	2.18	0.022	1.12	4.26
Pre-school children	2.32	0.022	1.13	4.77
Contact with pets with diarrhoea	2.19	0.005	1.27	3.77
Visiting a farm	2.05	0.03	1.07	3.93
Visiting a farm in summertime	0.24	0.03	0.07	0.87
The winter	0.49	0.012	0.28	0.85
Summertime	1.01	0.94	0.70	1.48
Organic meats	1.14	0.76	0.49	2.68
Age	0.99	0.229	0.98	1.01
Gender	1.32	0.106	0.94	1.85

* Odds ratio; † exact confidence interval.

diarrhoea or to have visited a farm in the 2 weeks before the onset of symptoms.

Other illness in the community

Of the 3489 cases of *C. jejuni* infection reported in the first year of the study, 333 (10% reported knowledge of an individual outside the household with a similar illness. Of these, 10 cases (10/333) reported that the other ill individual or individuals had a date of onset greater than 1 week from the case. These cases were excluded, leaving 323 'cases' and 3048 'controls'.

Cases were, on average, younger (mean 32.5 years) than controls (mean 39 years) (*t* test, $P < 0.001$) and were more likely to be female (56.7 vs. 49.5%; $\chi^2 P = 0.01$). There was no difference between these groups of cases with regard to length of illness (mean 11 days each; *t* test, $P = 0.9$) or admission to hospital (10.8 vs. 10.5%; $\chi^2 P = 0.8$).

Exposures in the fortnight prior to illness (single risk variable analysis)

Cases were more likely to be intermediate non-manual workers (e.g. teachers, nurses, etc.) and farmers than controls (Table 3). They were more likely to be female and were more likely to have travelled outside or within the United Kingdom in the 2 weeks before illness. They were more likely to report the consumption of organic vegetables, vegetarian foods, food in restaurants, unpasteurized milk or bottled water. They were more likely to report swimming, sailing or contact with animals.

Independent exposures in the fortnight prior to illness (logistic regression analysis)

Cases tended to be younger than controls and were more likely to be intermediate non-manual workers (Table 4). They were more likely to report eating in restaurants and consuming unpasteurized milk.

DISCUSSION

Data from the first year of a large, population-based sentinel surveillance scheme suggests that point source outbreaks of *C. jejuni* infection in England and Wales, either in the home or in the community, might be more common than was previously thought. Case-case comparisons have allowed us to identify independent factors which might expose several individuals to campylobacter infection at the same time.

In the majority of instances, we were unable to determine the aetiological agent responsible for illness in other individuals reported to be symptomatic at the same time as the cases. This could have implications for the specificity of our case definition, since in some instances other illness reported by cases in the home or the community might not have been acquired from a common point source or might have been aetiologically unrelated. We examined extensively the available epidemiological data and excluded those cases where the illness might have been secondary or aetiologically unconnected in order to minimize false positivity. Conversely, some cases might have represented true clusters while not necessarily being aware of other related illness. However, our questionnaire

Table 3. Risk exposures for illness in the community – single risk variable analysis (exposures with a $P < 0.1$ are shown)

Exposure	Percent exposed		OR*	P	95% CI†	
	'Cases'	'Controls'			Lower	Upper
South and West Devon District Health Authority	1.2	3.3	0.36	0.04	0.13	0.99
Increasing 10-year age group	—	—	0.86	<0.001	0.81	0.91
Intermediate non-manual workers	4.6	6.3	1.76	<0.001	1.30	2.37
Farmers (employers and managers)	0.7	0.1	9.52	0.006	1.33	68.0
Retired individuals	8.3	18.5	0.40	<0.001	0.26	0.61
Asian ethnicity	2.9	6.0	0.47	0.03	0.23	0.96
Travel abroad	23.8	18.5	1.37	0.02	1.04	1.80
Travel in the UK	18.6	14.2	1.38	0.04	1.01	1.88
Barbecued food	24.6	17.5	1.53	0.004	1.15	2.04
Lamb	37.1	44.3	0.74	0.02	0.58	0.95
Meat pies	19.4	29.0	0.59	<0.001	0.43	0.80
Organic vegetables	19.1	14.9	1.34	0.07	0.97	1.85
Vegetarian food	24.1	19.1	1.34	0.04	1.01	1.79
Eating in restaurants	65.7	53.4	1.67	<0.001	1.31	2.13
Unpasteurized milk	11.6	7.8	1.55	0.02	1.06	2.27
Bottled water	62.0	52.7	1.46	0.002	1.14	1.86
Swimming	27.7	18.8	1.65	<0.001	1.28	2.15
Sailing	3.6	1.7	2.08	0.03	1.07	4.05
Contact with animals	64.0	57.3	1.32	0.02	1.04	1.68
Contact with pet rodents	6.6	4.1	1.63	0.06	0.97	2.73

* Odds ratio; † exact confidence interval.

Table 4. Independent risk exposures for illness in the community (logistic regression model controlling for age, gender and season)

Exposure	OR*	P	95% CI†	
			Lower	Upper
Farmers (employers and managers)	3.89×10^9	—	—	—
Unpasteurized milk	2.15	0.002	1.33	3.49
Intermediate non-manual workers	1.49	0.045	1.01	2.19
Restaurants	1.40	0.036	1.02	1.92
Asian ethnicity	0.28	0.01	0.11	0.74
Meat pies	0.56	0.003	0.38	0.82
Age group (increasing)	0.82	<0.001	0.75	0.89
Male gender	0.75	0.059	0.55	1.01
Season	0.95	0.528	0.82	1.10

* Odds ratio; † exact confidence interval.

contained specific questions about other individuals with similar symptoms at the same time, and we would expect that most cases would be aware of other concurrent illness resulting from point source exposures, particularly among individuals in their own home.

Other illness in the household

Concurrent illness within the household setting might be less important than in the community in public health terms as the numbers affected will tend to be

smaller. However, there are still issues with regard to treatment and prevention, and our data suggest that simultaneous *C. jejuni* infection occurs more frequently in the household setting than in the community.

An association between the consumption of organic meats in the winter and other illness in the household might relate to a higher prevalence of *C. jejuni* in organic meats. In a study of *Campylobacter* spp. in 160 broiler flocks in Denmark, 100% of organic broiler flocks were positive, compared with 37% of conventional broiler flocks and 49% of extensive indoor broiler flocks [17]. The prevalence of exposure to organic meats was low, and the increased risk in the winter might relate to greater consumption of meat dishes, such as roasts, at this time of year [18]. We did not ask about the type of organic meat consumed. However, an accurate assessment of the risks associated with organic meats is needed, especially as the production [19] and consumption [20] of organic produce has increased dramatically in the United Kingdom recently.

The associations between pre-school and school children and other illness within the household might indicate selection bias. Individuals in households often share meals and activities, therefore it is possible that several members may become infected by a single contamination event. However, whilst symptomatic adults might not present to general practitioners (GPs), it is more likely that symptomatic children would be taken to their GP [21].

Contact with pets with diarrhoea was suspected as a source of campylobacter infection in man before campylobacters were recognized as important human pathogens [22]. Campylobacters have been isolated from a variety of domestic animals [23–27] and contact with animals has been implicated in several epidemiological studies of campylobacter infection [28–32]. Pets are often regarded as members of the household, and close contact with them increases the likelihood of disease transmission [33]. Owners, and possibly more importantly the children of owners [30], need to be made aware that pets might be an important source of campylobacter and other enteric infections. This might best be achieved at the pet shop or veterinarian level.

The role of farm visits as a source of enteric disease has been highlighted by outbreaks and incidents of Vero cytotoxin-producing *Escherichia coli* (VTEC) O157 infection. Like VTEC O157 [34–36], campylobacters are shed intermittently by symptomatic [37]

and asymptomatic [38] farm animals and the infective dose for humans is low [5, 39]. Poor hygiene following contact with the farm environment might therefore lead to infection. Recent guidelines for the control of infection with VTEC O157 provide specific information for farms open to the public [36], and this advice applies equally to avoidance of campylobacter infection.

Other illness in the community

The consumption of unpasteurized milk has been associated with outbreaks of campylobacter infection in England and Wales [40–45]. Its inclusion here is therefore unsurprising, but it might add weight to other observed associations. Raw milk for drinking remains on sale despite overwhelming scientific evidence [46–49] about the risks associated with its consumption. Those who drink it believe that the health benefits outweigh the risks, although these have not been demonstrated [50]. Under current UK legislation [51] raw milk for drinking should be free from pathogenic micro-organisms. Enforcement, through inspection and testing by food authorities, is done at a frequency considered necessary to ensure that the requirements of the regulations are complied with. If raw milk for drinking is to remain on sale (several attempts by the Government to ban its sale have been unsuccessful [52]) then this frequency needs to be increased.

The association between eating in restaurants and other illness in the community might relate to poor hygiene in the commercial catering environment. Outbreaks of campylobacter infection have been shown to be associated with commercial catering premises [3, 4] and epidemiological studies of sporadic disease have linked chicken prepared by or eaten in a commercial food establishment with infection [53–55]. Caterers need to be made aware that contamination of the hands and the environment with campylobacters can occur whilst preparing raw meat dishes [56, 57], and this contamination can be spread to ready-to-eat foods. An assessment of the risks involved in each step of the food preparation process, based on the principles of Hazard Analysis and Critical Control Points and in line with UK food safety legislation [58], is recommended if infection associated with, and poor consumer confidence in [59], these premises is to be avoided.

Older cases of *C. jejuni* infection were less likely to report other illness in the community. This might

be artefactual. The questionnaires for infants and younger children are answered by their parents who might be aware of other illness through playgroups, schools, etc.

The independent inverse associations identified in this study might point towards poor outbreak recognition rather than sources of sporadic infection. Laboratory reports underestimate the true incidence of infection by a factor of eight [2], therefore a large number of people must be infected from the same source for that source to be identified amongst laboratory-confirmed cases.

Finally, a note should be made on the independence of subjects included in this analysis. Ideally, each true cluster of disease would be represented by a single case. It is possible that some cases were, in fact, part of the same clusters, and this could have led to an over-estimation of effects due to factors related with those clusters.

CONCLUSION

Concurrent illness in the home and/or the community occurred more frequently than might have been expected, based on previous publications. The results of these analyses are plausible in that they highlight exposures which would have affected more than one member of a family or a community at the same time. Prevention of campylobacter infection requires that better methods of outbreak detection are developed, which in turn should lead to a better understanding of risk factors.

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