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The Public Health Laboratory Service national case-control study of primary indigenous sporadic cases of campylobacter infection

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SUMMARY

The aetiology of sporadic campylobacter infection was investigated by means of a multicentre case-control study. During the course of the study 598 cases and their controls were interviewed.

Conditional logistic regressional analysis of the data collected showed that occupational exposure to raw meat (odds ratio [OR] 9·37; 95% confidence intervals [CI] 2·03, 43·3), having a household with a pet with diarrhoea (OR 2·39; CI 1·09, 5·25), and ingesting untreated water from lakes, rivers and streams (OR 4·16; CI 1·45, 11·9) were significant independent risk factors for becoming ill with campylobacter. Handling any whole chicken in the domestic kitchen that had been bought raw with giblets, or eating any dish cooked from chicken of this type in the home (OR 0·41–0·44; CI 0·24, 0·79) and occupational contact with livestock or their faeces (OR 0·44; CI 0·21, 0·92) were significantly associated with a decrease in the risk of becoming ill with campylobacter.

INTRODUCTION

The number of confirmed cases of campylobacter enteritis reported to the Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre (CDSC) by laboratories in England and Wales has risen steadily since suitable selective media became widely available in the late 1970s [1, 2]. Campylobacters are currently the most commonly reported microbial cause of acute gastroenteritis in England and Wales and have been since 1981. In 1994 CDSC received over 40000 reports of laboratory confirmed cases of campylobacter enteritis [3]. Less than 1% of cases reported to CDSC are part of known outbreaks.

It has long been suspected that campylobacter enteritis is a food-borne infection, as healthy food animals are intestinal carriers of the organism and a number of studies have shown that campylobacters are frequently found on raw meat, particularly chicken [4, 5], and in raw milk [6]. Indeed chicken [7, 8] and raw [6] or inadequately treated [9] milk have been the most commonly implicated vehicles of infection in recorded outbreaks. Outbreaks have also been associated with the consumption of untreated water [10]. Infection has been shown to be associated with contact with dogs, especially puppies with diarrhoea [11]. Recent studies have demonstrated that the consumption of doorstep delivered milk that had been pecked by magpies or jackdaws [12, 13], is a risk factor.

A multicentre case-control study was carried out, between May 1990 and January 1991, to investigate the importance of a variety of risk factors in the aetiology of sporadic campylobacter infection. The risk factors addressed included: occupational exposure to livestock or raw meat; consumption and handling of chicken and other meats; consumption of raw and treated milk; consumption of treated and untreated water; and contact with household pets.

METHODS

Study design

The investigation was a multicentre case-control study of laboratory confirmed cases of primary, home-acquired, sporadic infection with *Campylobacter jejuni/coli*, using a standard questionnaire. The questionnaires were administered over the telephone by a small number of interviewers based in 11 Public Health Laboratories: Bath; Birmingham; Cambridge; Chelmsford; Epsom; Gloucester; Hereford; Liverpool; Newcastle; Rhyl; and Southampton. Each interviewer was supplied with a comprehensive set of interview guidelines before the start of the study.

Subjects

Cases were defined as people with abdominal pain, or acute diarrhoea, from whose faeces *Campylobacter jejuni/coli* had been cultured. Specimens were sent to Manchester PHL for serotyping. At the beginning of each week laboratory coordinators would decide how many cases were to be selected for interview on the basis of available time and resources. These cases were selected systematically from the sum total of primary, home-acquired, sporadic cases identified by the laboratory coordinator each week between May 1990 and January 1991.

Controls were nominated by cases, or by parents where children were affected. Controls were matched for age, sex (if over 10 years old), and geographical location of residence or place of work. Case-control sets were included for analysis provided that one control questionnaire was returned for each case. Every effort was made to interview two controls for each case or three when possible.

Questionnaire details

The following information was sought from cases: demographic details, including age, sex, occupation, place of residence; recent foreign travel, i.e. travel outside the UK and the Republic of Ireland in the 10 days prior to the onset of illness; household details, including diarrhoeal illness in other members of the household; clinical details; contact with pets, livestock and wildlife; ingestion of untreated water; and consumption of chicken, barbecued meat, milk and unboiled tap water. The clinical details section was not included on control questionnaires. Controls were asked for details relating to the 10 days prior to the onset of illness in the case to whom they were matched.

Statistics

The data were analysed using conditional logistic regression techniques for matched case-control studies [14]. Crude and adjusted odds ratios and 95% confidence intervals of individual factors were obtained. Statistical significance

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Table 1. *Demographic characteristics*

	Study subjects		Laboratory reports to CDSC
	Cases (%)	Controls (%)	1990 (%)
Sex			
Male	305 (51·0)	365 (49·5)	18077 (52·3)
Female	293 (49·0)	373 (50·5)	15541 (45·0)
NS*			938 (2.7)
Age			
0–4 y	69 (11·5)	87 (11·8)	5060 (14·6)
5–14 y	51 (8·5)	64 (8·7)	2289 (6·6)
15–24 y	92 (15·4)	105 (14·2)	5647 (16·3)
25–44 y	217 (36·3)	273 (37·0)	11043 (32·0)
> 44 y	168 (28·1)	209 (28·3)	7696 (22·3)
NS*	1 (0·2)	0 (0·0)	2821 (8·2)
Total	598	738	34556

* NS, Not stated.

was assessed using the likelihood ratio test. Analyses were performed using the software package GLIM4 [15].

RESULTS

The age distribution of subjects in the study was similar to that of cases of campylobacter infection reported to CDSC in 1990 (Table 1). Completed questionnaires from case-control sets were returned for 68% of eligible laboratory confirmed cases. Response rates from individual laboratories were in the range 42–84%.

Single variable analysis

Four factors were found to be associated with an increase in risk for becoming ill with campylobacter (Table 2), these were: occupational exposure to raw meat ($P = 0{\cdot}002$); contact with pets with diarrhoea ($P = 0{\cdot}005$); consumption of chicken at barbecues ($P = 0{\cdot}004$); and ingestion of untreated water while participating in recreational activities ($P = 0{\cdot}013$). Three factors were found to be associated with a decrease in risk for becoming ill with campylobacter, these were: occupational exposure to animals or faeces ($P = 0{\cdot}035$); animal contact outside the home ($P = 0{\cdot}005$); and consumption at home or handling in the domestic kitchen of chicken that had been bought whole, raw and with giblets ($P < 0{\cdot}001$).

Multivariable analysis

In order to adjust for confounding, a full regression modelling analysis was performed using all the variables included in the single variable analysis. A number of variables were found to contribute little to making the model fit the data better, and were excluded from subsequent analyses. These were: consumption or handling chicken that had been bought ready cooked; consumption of chicken away from home, but not at barbecues; and consumption of sausages and kebabs at barbecues. A final main effects model was fitted using the

Table 2. *Single variable analysis – crude odds ratios and 95% confidence intervals*

Variable	Exposure group	Cases*	Controls*	Odds ratios (95% CI)	*P*-value
Occupational group	Contact with raw meat	28	7	9.24 (2·84, 30·0)	
	Contact with animals/ faeces	33	59	0·55 (0·32, 0·96)	< 0·01
	All other occupations	495	618	1·00	
Contact with pets at home	Yes – pets had diarrhoea	35	19	2·41 (1·30, 4·46)	
	Yes – pets healthy	318	412	0·97 (0·76, 1·25)	< 0·01
	No	244	306	1·00	
Contact with other animals	Yes	273	393	0·72 (0·57, 0·91)	< 0·01
	No	320	338	1·00	
Consumption/handling of chicken cooked and eaten at home	With giblets	97	167	0·52 (0·36, 0·73)	
	Without giblets	238	282	0·81 (0·62, 1·07)	< 0·01
	None	214	217	1·00	
Consumption of ready cooked chicken at home	Portions	64	77	1·00 (0·70, 1·44)	
	Whole and portions	11	19	0·79 (0·37, 1·67)	0·82
	None	484	592	1·00	
Consumption of hot chicken away from home	Well cooked	111	146	0·90 (0·67, 1·21)	
	Undercooked	9	4	4·65 (0·95, 22·8)	0·07
	None	362	434	1·00	
Consumption of cold chicken away from home	Yes – well cooked	24	26	1·14 (0·62, 2·11)	
	Yes – undercooked	2	0	297 (0·00, > 1000)	0·23
	No	331	392	1·00	
Consumption of barbecued chicken	Yes – well cooked	37	50	0·95 (0·59, 1·53)	
	Yes – undercooked	12	2	16·0 (2·36, 108·6)	< 0·01
	No	517	643	1·00	
Consumption of barbecued beef	Yes – well cooked	35	46	1·06 (0·64, 1·76)	
	Yes – undercooked	5	0	824 (0·00, > 1000)	0·01
	No	521	640	1·00	
Consumption of barbecued pork	Yes – well cooked	14	29	0·53 (0·26, 1·07)	
	Yes – undercooked	1	0	109 (0·00, > 1000)	0·10
	No	535	644	1·00	
Consumption of barbecued sausages	Yes – well cooked	55	74	0·89 (0·59, 1·34)	
	Yes – undercooked	3	3	1·72 (0·30, 8·65)	0·67
	No	513	623	1·00	
Consumption of barbecued kebabs	Yes – well cooked	14	19	0·88 (0·44, 1·77)	
	Yes – undercooked	2	1	2·56 (0·23, 29·1)	0·70
	No	528	647	1·00	
Consumption of milk	Yes – heat treated	358	458	0·91 (0·70, 1·18)	
	Yes – untreated	11	5	3·24 (0·86, 12·2)	0·11
	No	210	251	1·00	
Water ingested from rivers, etc.	Yes	23	11	2·60 (1·22, 5·52)	0·01
	No	525	660	1·00	
Consumption of cold tap water	Yes	458	558	1·05 (0·80, 1·38)	0·71
	No	135	172	1·00	

* The figures presented in this table show the numbers falling into each category without taking matching into account.

variables shown in Table 3. Occupational exposure to raw meat (e.g. through working as a chef or butcher), living in a household with a pet with diarrhoea, and ingesting untreated water from lakes, rivers and streams were all found to be significant independent risk factors for becoming ill with campylobacter (Table 3).

Table 3. *Multivariable analysis – adjusted odds ratios and 95% confidence intervals*

Variable	Exposure group	Odds ratios (95% CI)	*P*-value
Occupational group	Contact with raw meat	9·37 (2·03, 43·3)	
	Contact with animals/faeces	0·44 (0·21, 0·92)	< 0·001
	All other occupations	1·00	
Contact with pets at home	Yes – pets had diarrhoea	2·39 (1·09, 5·25)	
	Yes – pets healthy	1·09 (0·77, 1·53)	0·09
	No	1·00	
Contact with other animals	Yes	0·78 (0·58, 1·06)	0·11
	No	1·00	
Consumption/handling of chicken cooked and eaten at home	Frozen – with giblets	0·41 (0·24, 0·79)	
	Fresh/frozen – with giblets	0·44 (0·24, 0·79)	< 0·001
	Frozen – no giblets	0·62 (0·37, 1·04)	
	Fresh/frozen – no giblets	1·21 (0·84, 1·74)	
	None	1·00	
Consumption of barbecued chicken	Yes – well cooked	1·53 (0·65, 3·60)	
	Yes – undercooked	4285 (0·00, > 5000)	0·01
	No	1·00	
Consumption of barbecued beef	Yes – well cooked	1·60 (0·66, 3·91)	
	Yes – undercooked	767 (0·00, > 5000)	0·13
	No	1·00	
Consumption of barbecued pork	Yes – well cooked	0·29 (0·08, 1·06)	
	Yes – undercooked	0·00 (0·00, > 5000)	0·16
	No	1·00	
Consumption of milk	Yes – heat treated	0·85 (0·61, 1·18)	
	Yes – untreated	5·03 (0·78, 32·6)	0·10
	No	1·00	
Water ingested from rivers, etc.	Yes	4·16 (1·45, 11·9)	0·01
	No	1·00	

Subjects were asked if chicken that had been cooked and eaten in the home had been bought fresh or frozen, with or without giblets, as whole chicken or in portions. Analysis of the data showed that handling any whole chicken bought raw with giblets in the domestic kitchen, or eating any dish cooked from chicken of this type in the home was significantly associated with a decrease in the risk of becoming ill with campylobacter (Table 3). Occupational contact with live animals or with faecal samples (e.g. through farming, veterinary practice, medicine or microbiology) was also significantly associated with a decrease in risk (Table 3).

In the single variable analysis consumption of chicken at barbecues was found to be associated with an increase in the risk of becoming ill with campylobacter; however it was found to have no effect when other variables were taken into consideration. The remaining factors were found to have no significant effect on the risk of becoming ill with campylobacter. There was no evidence of age, sex, laboratory or interviewer interacting with any of the factors under investigation.

Analysis of the serotyping data did not indicate any relationships between rates of infection with individual campylobacter serotypes and particular risk factors.

DISCUSSION

The study demonstrated associations between campylobacter enteritis and a number of risk factors which have been demonstrated in previous studies: handling and preparation of raw meat [16]; exposure to pets with diarrhoea [11];

and ingestion of untreated water [10]. More surprisingly, the study also showed that both the consumption of chicken in the home and occupational contact with live animals or with faecal samples were significantly associated with a decrease in the risk of acquiring infection. We have considered the following possible explanations for our findings.

(i) Systematic bias

Biases may be introduced when controls are nominated by cases. False associations may be created or true associations obscured, if sufficient cases nominate controls on the basis of their likely exposure to particular risk factors. For this to happen cases would need to have time to guess the hypotheses being tested. Given that the cases were asked to nominate controls at the end of a telephone interview, without forewarning, it is highly unlikely that they would have sufficient time to make such judgements.

(ii) Confounding

Associations may exist between certain variables and other characteristics which were protective but could not be determined from the data (e.g. people who buy whole rather than portioned chicken may have higher levels of kitchen hygiene). There is no evidence for this.

(iii) A causal link

Only people who were free of symptoms in the month before interview were eligible to be included as controls. It is possible that the control population included people who were symptom free because their frequent exposure to sources of campylobacter made them more likely to be immune. This phenomenon could also explain the protective effects described in other studies. A small case-control study of laboratory confirmed cases of sporadic campylobacter infection carried out in Colorado, USA, in 1981 found chicken consumption to be more common among controls than cases [17]. In 1989 the national case-control study of *Salmonella enteritidis* phage type 4 infection also found consumption of chicken meat to be protective [18]. A study of verocytotoxin producing *Escherichia coli* (VTEC) infection on dairy farms in Ontario demonstrated a negative association between consumption of hamburgers and *E. coli* O157:H7 infection [19]. Hamburgers are a well known source of VTEC infection [20] just as chicken meat is for campylobacter and *S. enteritidis* PT4. The exposure is a risk factor for the susceptible fraction of the population, perhaps even the majority, but appears protective because the controls are not representative of the population as a whole, they are more likely to be immune. There is evidence from other studies that people who are repeatedly exposed to campylobacters do indeed develop immunity [21]. The use of convenient and reliable tests of immunity would enhance the value of further studies, which could confirm our hypothesis that although poultry meat may be a risk factor to susceptibles, its regular consumption confers immunity. The results of this large national study support the hypothesis that immunity in controls can exert important effects on studies of the epidemiology of infectious disease and that these effects are powerful enough not only to influence the results of smaller local studies but also those of large multicentre investigations.

Typing schemes are available for campylobacters, but the current epidemiological utility of these schemes is difficult to assess. In order for a scheme to be useful the typing must reflect real differences in the natural history of the organism. An epidemiologically useful scheme would distinguish between organisms of different levels of virulence, host preference, geographical distribution, etc. as well as in the occurrence of a particular genotypic or phenotypic marker. More complete typing by methods already available as well as research into novel methods is essential if we are to learn more about the epidemiology of campylobacter enteritis.

Further studies which take into account human immune status to campylobacter infection, and epidemiologically useful distinctions between campylobacter sub-groups would clearly be worthwhile. Clarification of both of these microbiological aspects is vital to the success of future epidemiological studies.

The study has confirmed that occupational exposure to raw meat, pets with diarrhoea and untreated water are still important risk factors and suggested that naturally acquired immunities may play an important role in the epidemiology of campylobacter infection.

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