Risk Factors for Sporadic Giardiasis: A Case-Control Study in Southwestern England

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To investigate risk factors for sporadic infection with *Giardia lamblia* acquired in the United Kingdom, we conducted a matched case-control study in southwest England in 1998 and 1999. Response rates to a postal questionnaire were 84% (232/276) for cases and 69% (574/828) for controls. In multivariable analysis, swallowing water while swimming (p<0.0001, odds ratio [OR] 6.2, 95% confidence intervals [CI] 2.3 to 16.6), recreational fresh water contact (p=0.001, OR 5.5, 95% CI 1.9 to 15.9), drinking treated tap water (p<0.0001, OR 1.3, 95% CI 1.1 to 1.5 for each additional glass per day), and eating lettuce (p=0.01, OR 2.2, 95% CI 1.2 to 4.3) had positive and independent associations with infection. Although case-control studies are prone to bias and the risk of *Giardia* infection is minimized by water treatment processes, the possibility that treated tap water is a source of sporadic giardiasis warrants further investigation.

Giardia lamblia, a flagellate waterborne protozoan parasite, is a common cause of gastrointestinal disease in industrialized and unindustrialized countries (1). Most information on risk factors for giardiasis has come from investigation of outbreaks. Water is the most frequently identified route of transmission (1,2), through drinking contaminated tap water (3,4) or recreational exposure in lakes, rivers, or swimming pools (5). Person-to-person spread is well documented in day-care centers and among male homosexuals (6,7), and food may also be a vehicle of infection (8).

The relative contribution of these routes of transmission to sporadic cases of giardiasis is unknown, and further studies have been recommended in the United States (9). In the U.K., recreational exposure to fresh water and swimming pools has been identified as a possible risk factor (10–12), as well as travel to developing countries (11). We set out to determine risk factors for giardiasis in residents of southwest England who had not recently traveled outside the U.K.

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Methods

Our study was conducted from April 1, 1998, to March 31, 1999 in southwest England, including Cornwall and Isles of Scilly, Devon, Somerset, Dorset, Wiltshire, Hampshire, Isle of Wight, Avon, Gloucestershire, and Herefordshire. Laboratories used for the study were the microbiology laboratories (managed by National Health Service trust or Public Health Laboratory Service) in the study area that routinely screened for *Giardia* cysts in all stool specimens submitted from persons with history of diarrhea. Study laboratories were located in Torbay, Exeter, Yeovil, Dorchester, Poole, Bournemouth, Salisbury, Basingstoke, Winchester, Portsmouth, Newport (Isle of Wight), Weston-super-Mare, Bristol/Bath, Frenchay, Cheltenham, and Hereford. All microbiology laboratories in the study area that fulfilled the study criteria (16/24) agreed to participate. Ethical approval for the study was obtained from the Public Health Laboratory Service Ethics Committee, the Southwest Multicentre Research Ethics Committee, and 16 Local Research Ethics Committees.

Case-patients were defined as residents of the study area with a history of diarrhea and *Giardia* cysts in their stool specimen seen by light microscopy (13) in the study period. Case-patients were excluded if they had traveled outside the U.K. in the 3-week period before onset of diarrhea or if a household member had diarrhea in the 3-week period before the patient's onset of diarrhea. Controls were persons registered at the same general practice as patients, of the same gender, and in the same broad age band (0–5 years, 6–15 years, ≥16 years). Controls were excluded if they had traveled outside the U. K. during the 3 weeks before interview or if they had diarrhea in the 3 weeks before interview.

The study questionnaire was derived from an instrument used in a case-control study of cryptosporidiosis in the north of England (S. Goh, pers. comm.). The questionnaire covered personal details, recent illness, travel, water contact, water and food consumption (food history focusing on dairy produce, salads, fruit), and contact with animals, farms, and day nurseries. Adults were asked for details of occupation. The questionnaire was modified from a pilot study; the wording of some questions was simplified, and a question about previous infection or treatment of *Giardia* infection was added. Patients were asked about exposures in the 3 weeks before onset of illness, and controls were asked about exposures in the 3 weeks before completion of the questionnaire. In questions about drinking unboiled tap water and bottled water, patients and controls were both asked about usual consumption patterns.

Cases were reported on identification to the principal researcher by fax or post. Health authorities, through the consultant in communicable disease control, randomly selected three controls for each case selected from the Health Authority population age-sex register. If the general practitioner had no objection to contacting patients and controls, the questionnaire was sent out with a covering letter. One month after the first questionnaire was posted, nonresponders were sent one reminder.

A required sample size of 192 cases was estimated by using Generalised Linear Interactive Modelling (GLIM) (14). This size was based on a case-control ratio of 1:3, with 95% confidence and 80% power to detect an odds ratio (OR) of at least 3 for the variable under investigation. Data were double entered onto a microcomputer, and single variable conditional logistic regression was carried out by using GLIM (15). Variables with $p<0.2$ in the single variable analysis were then included in a multivariable conditional logistic regression analysis. A series of models were fitted; clearly nonsignificant terms were eliminated to maximize the number of subjects that could be used in the regression modeling. As a large number of observations were "don't know" or "missing" for the "swallowing water while swimming" variable, an extra level was included for this variable. This addition resulted in a final main effect model that included 655 subjects (95% of the 689 available). All the 2-way interactions were tested, including those involving age and sex.

Results

Questionnaires were returned from 232/276 case-patients and 574/828 controls, response rates of 84% and 69%, respectively. Two additional patients were not included because their general practitioners did not agree to participate in the study. After the exclusion criteria were applied, data from 192 cases and 492 controls were available for analysis, a ratio of 1:2.5. Of the 40 case-patients excluded, 18 had traveled outside the U.K., 15 were possible secondary case-patients, and 7 did not report diarrhea. Of the 82 excluded controls, 43 reported diarrhea, 38 had traveled outside the U.K., and reasons for exclusion were missing for one. The incidence of giardiasis fulfilling the study criteria was 4.7/100,000 during the 12-month study period. Seasonal variation was not marked, and no outbreaks were detected during the study. Cases were most frequent in the 30- to 39-year age group. Although frequency matching had been used to obtain controls with similar age distribution to the case-patients, some differences were observed in those remaining for analysis: 17% of the patients and 22% of the controls were <16 years of age. Eighty-seven (44%) of the case-patients were male, and 109 (56%) were female. Among the nonresponders, a higher proportion were male (33/44,) but the age distribution was similar. Social class distribution was similar in adult case-patients and controls ($p=0.1$).

By definition, all case-patients (192) had diarrhea. One hundred and forty-eight (77%) case-patients had abdominal pain, 73 (38%) reported vomiting, 53 (28%) had a fever, 12 (6%) noted blood in stools, and 90 (47%) reported other symptoms, including tiredness, weight loss, nausea, and headache. The median reported duration of illness was 21 days (range 1–305). Thirteen patients reported that they were still unwell at the time of completing the questionnaire.

In the single variable analysis, a dose-response relationship existed between reported number of glasses of tap water usually drunk per day and risk of illness ($p<0.0001$, Table 1). No evidence of a dose-related response existed for those who drank only bottled water. The homes of >98% of patients and controls were on public water supply (provided by one of the seven statutory water companies in the study area). Most case-patients (73%) were supplied by the same water treatment works as their matched controls. Home water supply was purely surface water for 40% of cases and 41% of controls, and purely ground water for 39% of cases and 33% of controls; data on water supply at work were not available. Several exposures relating to swimming in chlorinated water and fresh water contact were significantly associated with illness (Table 2). In a wide range of questions on food consumption, eating lettuce was the only variable significantly ($p<0.05$) associated with infection (OR 2.3, 95% confidence interval [CI] 1.3 to 4.1, $p=0.003$). Visiting a farm was more frequent among case-patients (OR 2.2, 95% CI 1.2 to 4.1, $p=0.01$), but none of the associations with specified animal exposures (dogs, cats, horses, cows, sheep) was statistically significant. Case-patients were more likely to have contact with a nursery (OR 2.2, 95% CI 1.2 to 4.2, $p=0.01$).

In the multivariable analysis, swallowing water while swimming, recreational contact with fresh water, dose response to drinking tap water, eating lettuce, and not eating ice cream were independently associated with illness (Table 3). For swallowing water while swimming, the "don't know/ missing" category had an OR of 5.3 (95% CI 1.9 to 14.8). If analysis of the water swallowing variable was restricted to those who specified chlorinated water, the association remained highly significant in the model ($p=0.006$, OR 3.9, 95% CI 1.3 to 11.4). Attributable fractions were estimated as 14% for swallowing water, 9% for fresh water contact, 35% for drinking three or more glasses of tap water per day, and 40% for eating lettuce.

Discussion

We found an association between drinking tap water and giardiasis in persons who had not recently traveled outside the U. K. This finding had a high level of statistical significance and was unexpected. U.K. public water supplies are thought to be at low risk for transmitting *Giardia* infection because of the lower resistance of *Giardia* cysts to chlorination compared with *Cryptosporidium* oocysts (16,17), their easier removal by

Table 1. Single variable analysis of risk factors for giardiasis: drinking water exposures

Risk factor		Cases (n=192)	Controls (n=492)	Matched odds ratio (95% CI)[a]	p value
Consumed tap water	No	17	79		
	Yes	174	410	2.3 (1.1 to 4.9)	0.02
Usual no. of glasses of tap water consumed per day (glass=approx 1/3 pint)	0.0	17	79		
	0.5–1.0	22	71		
	1.5–2.0	52	150		
	2.5–3.0	23	46		
	3.5–4.0	23	41		
	4.5–5.0	20	41		
	>5.0	33	61	1.2 (1.1 to 1.4)[b]	<0.0001
Consumed bottled water	No	154	406		
	Yes	38	83	1.6 (0.9 to 2.9)	0.1
Usual no. of glasses of bottled water consumed per day	0	154	406		
	1	12	29		
	2	19	32		
	3	5	13		
	4	1	8	1.2 (0.9 to 1.6)[b]	0.3
Used water filter at home	No	157	387		
	Yes	34	104	0.9 (0.5 to 1.7)	0.8
Type of water supply	Public	187	483		
	Private	3	3	0.05 (0.002 to 1.11)	0.04
Had a disruption in the water supply	No	124	447		
	Yes	6	11	3.6 (0.6 to 20.8)	0.2

[a]CI, confidence intervals.
[b]For each additional glass.

filtration (18), and the few outbreaks of giardiasis attributed to drinking water (19). A causal link cannot, however, be excluded, as *Giardia* cysts have been frequently found in U. K. surface waters (D. Sartory, pers. comm.), and outbreaks attributed to chlorinated water in the United States are well documented (3,20). The association with drinking water might have been overestimated because of changes in water consumption after illness or because of bias. Information bias is a recognized problem in case-control studies; such bias was not found, however, in a case-control study conducted during and after a giardiasis outbreak in Nevada (21). The matched design of our study reduced the risk of error from confounding factors but also resulted in close matching on home water supply such that assessing the effect of drinking water quality indicators on outcome was not possible.

Another new finding was an increased risk for giardiasis associated with eating lettuce (green salad). A true risk is certainly plausible, as irrigation and fertilization practices may lead to contamination with *Giardia* and other organisms (22,23). Outbreaks of giardiasis in the United States have been attributed to eating salad contaminated by food handlers (24). The negative association between illness and eating ice cream is unlikely to represent a true protective effect. This finding may have arisen from study biases, but preference for ice cream could simply be a marker for those who are less likely to eat salads, which are at higher risk of *Giardia* contamination. An apparently false protective effect of soft drinks has been observed in outbreaks of cryptosporidiosis attributed to tap water (25).

The association between giardiasis and swallowing water while swimming is not surprising; several outbreaks of giardiasis have been linked with exposure to chlorinated water in swimming pools (3,5). If those who did not know if they swallowed water were more likely to have actually swallowed

Table 2. Single variable analysis of risk factors for giardiasis: recreational water exposures

Swimming and related activities by location and frequency:		Cases (n=192)	Controls (n=492)	Matched odds ratio (95% CI)[a]	p value
Swimming anywhere	No	123	406		
	Yes	66	85	3.9 (2.2 to 7.1)	<0.0001
Swallowing water while swimming	No	132	428		
	Yes	26	33	6.6 (2.5 to 17.6)	0.0001
Frequency of swimming	0	123	406		
	1–2	29	44		
	3–4	22	19		
	5–6	6	10		
	7–8	4	11	1.3 (1.1 to 1.5)[b]	0.002
Chlorinated water exposure					
Swimming	No	149	434		
	Yes	43	58	2.7 (1.4 to 5.0)	0.002
Swallowed water	No	174	464		
	Yes	18	28	2.4 (0.9 to 6.0)	0.07
Head immersion	No	156	443		
	Yes	36	49	2.5 (1.3 to 5.0)	0.009
Fresh water exposure	No	172	469		
	Yes	20	23	5.1 (2.0 to 12.5)	0.0003
Swallowed water	No	191	491		
	Yes	1	1	3.9 (0.1 to 136)	0.4
Head immersion	No	188	489		
	Yes	3	2	26.6 (1.2 to 572)	0.02
Sea water exposure	No	187	486		
	Yes	5	6	1.2 (0.2 to 8.4)	0.9

[a]CI, confidence intervals.
[b]For each additional visit.

water, this could explain the high OR in this category. A higher risk of exposure to recreational fresh water accords with results of other studies (10,12,26). By contrast with studies from the United States (26,27), contact with children's nurseries was not found to be an independent risk factor. In New Zealand, where the attack rate among young children is relatively high, an increased risk was found in adults who changed infants' diapers (28), and information on household contact with young children should be sought in further studies. No risk was identified from contact with animals. One case-control study in the east of England showed associations with exposure to farm animals and pets, particularly pigs, dogs, and cats (29); other studies have not found such associations (26,30). The microbiologic evidence for zoonotic transmission is similarly conflicting (2). Although no questions were included on sexual behavior, the similar numbers of male and female cases in the study does not support a hypothesis that male homosexual behavior was an important method of transmission in this population.

The incidence of laboratory-reported cases of *Giardia* infection in England and Wales was $8.2/10^5$ in 1998–2000 (31), and a study of infectious intestinal disease in England in 1993–95 suggested that the true incidence rate of giardiasis was around $50/10^5$ (32). *Giardia* infection may be asymptomatic in children, but infection in adults usually leads to acute severe gastrointestinal illness that may be prolonged (median duration 3 weeks in our study) and may lead to chronic malabsorption and weight loss. In marked contrast to most other gastrointestinal infections, giardiasis can be successfully treated with drugs such as metronidazole (1). Higher awareness of non–travel-associated infection is needed in primary care and diagnostic microbiology laboratories so that correct treatment

Table 3. Multivariable analysis of risk factors for giardiasis

Exposure	Odds ratio (95% CI)[a]	p value
Swallowed water while swimming	6.2 (2.3 to 16.6)	<0.0001
Recreational fresh water contact	5.5 (1.9 to 15.9)	0.001
Each additional glass of tap water consumed per day	1.3 (1.1 to 1.5)	<0.0001
Ate lettuce	2.2 (1.2 to 4.3)	0.01
Ate ice cream	0.4 (0.2 to 0.7)	0.002

[a]CI, confidence intervals.

can be given and disease incidence measured more accurately. A causal link between exposure to treated drinking water and sporadic giardiasis would have considerable public health importance but cannot be established on the basis of this study. Further case-control studies, in conjunction with assessment of drinking water quality that includes examination for *Giardia* cysts, would help to resolve this issue.

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