SHORT REPORT

Putative household outbreaks of campylobacteriosis typically comprise single MLST genotypes

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SUMMARY

During a 15-month period in Scotland a small but important number of human Campylobacter cases (3·2%) arose from 91 putative household outbreaks. Of the 26 outbreaks with known strain composition, 89% were composed of the same MLST which supports the potential use of MLST in public health epidemiology. The number of cases associated with household outbreaks is much larger than general outbreaks and there is some evidence to indicate that there may be secondary transmission, although this is relatively rare.

Key words: *Campylobacter*, epidemiology, genotyping, infectious diseases, multi-locus sequence typing, outbreaks.

Campylobacter is the leading cause of bacterial intestinal infection in the developed and developing world [1], and infections appear predominantly sporadic. The most common exceptions are household outbreaks, which comprise 3–5% of infections as reported in Denmark [2] and in Wales [3].

Two-thirds of family-associated outbreaks in a region of South Wales (1996–1999) [3] each contained a single strain, as defined by serotyping and phage-typing. But the identification of *Campylobacter* outbreaks is hindered by the co-occurrence of different *Campylobacter* strains in individual outbreaks [4]

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and the lack of agreed portable typing methodologies [2].

Multi-locus sequence typing (MLST) is a genotypic strain-typing method based on DNA sequences from seven housekeeping genes [5] that has been applied to many bacterial species. The sequence types (STs) generated can then be used to compare strains and provide molecular evidence for identifying outbreaks. The aims of this study were to (i) identify putative household outbreaks in cases reported to national surveillance in Scotland, (ii) characterize their further epidemiological attributes, and (iii) evaluate genotypic strain composition as a means of confirming these outbreaks.

During July 2005 to September 2006, 5831 cases of human campylobacteriosis were reported to national surveillance in Scotland. *Campylobacter* isolates, from

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Table 1. Epidemiological data for putative household outbreaks genotyped by MLST sequence type

Putative household outbreak			MLST type	Reported time difference between cases
	Age (yr)	Sex		
1	8	F	583	<1 week
	6	M	583	
2	57	F	5	<1 week
	60	M	5	
3	7	F	464	3–4 weeks
	4	M	464	2 21
	5 2	M F	21 21	2–3 weeks
5	45	M	21	2–3 weeks
	16	F	21	2-3 weeks
6	77	M	206	<1 week
	74	F	206	(1 Week
7	7	M	53	2–3 weeks
	5	M	53	
8	42	F	1365	<1 week
	1	M	2131	
9	3	F	273	3–4 weeks
	1	M	273	
10	16	F	21	<1 week
11	15	F	21	
	2	F	2030	<1 week
12	4	M	2030	.1 1
	12	M	2030	<1 week
13	10 36	M F	2030 400	1–2 weeks
	7	M	42	1-2 weeks
14	39	M	75	<1 week
	14	F	75	VI WEEK
15	42	M	267	<1 week
	41	F	962	
16	44	F	51	<1 week
	46	M	51	
17	5	M	53	<1 week
	3	M	53	
18	21	M	61	1–2 weeks
	50	M	61	
19 20	3	M	262	<1 week
	38	F	262	
	0	M	262	.11.
	72 72	F M	257 257	<1 week
21	41	M	257 257	<1 week
	40	F	257	\1 WCCK
22	33	F	45	<1 week
	6	M	45	VI WOOK
23	31	M	262	<1 week
	28	F	262	
24	82	F	52	<1 week
	88	M	52	
25	8	F	19	<1 week
	4	F	19	
26	7	M	475	1–2 weeks
	4	F	475	

reported human cases, were submitted from public health bacteriology laboratories and typed by MLST as previously described [6]. Linkage between epidemiological data (address, age, sex and date of report) and MLST type was achieved for 3713 cases. Putative household outbreaks were defined as ≥ 2 cases with the same residential address and family surname, and reporting dates within 28 days. Ninetyone such outbreaks were identified (86 with 2 cases, three with 3 cases and two with 4 cases), and these comprised 3.2% of all reported Campylobacter cases. According to a randomization test [7], these groups were significantly more frequent (P < 0.00001) than the 6.4 groups expected to occur by chance in the 2.29 million households in Scotland during the study period [8]. During this period >30-fold household outbreaks were reported than general outbreaks (n=3). This is of the same order of magnitude to that found in Denmark where >21-fold household outbreaks were reported than general outbreaks [2]. Further, it is worth noting that in Scotland the three general outbreaks comprised a total of 40 cases which suggests that there are about five times as many cases associated with household outbreaks. However, a larger study is required to confirm the robustness of this difference.

Twenty-six of these putative household outbreaks had complete MLST genotyping information (Table 1). In 23 (89%) of these putative household outbreaks the cases within each group shared the same ST, and this was significantly more often (P < 0.00001) than expected by chance (13%). The high frequency of strain matching within the putative household outbreaks resembled the strain composition of family-associated outbreaks in Wales [3]. From these results it can be hypothesized that the other five putative household outbreaks which contained different STs were caused by co-infection with different strains from the same source, e.g. food vehicle, as is known to have occurred in an outbreak attributed to chicken liver pâté [4].

The cases in each putative household outbreak showed the following differences in reporting dates: 62% were up to 1 week apart, 20% were 1–2 weeks apart and 18% were 2–4 weeks apart. The group at 2–4 weeks apart is suggestive of secondary infections, which are believed to be very rare in *Campylobacter* [1]. Further analyses based on date of onset rather than reporting date are needed to quantify the incidence of secondary infections more precisely. It would also be important to ensure that this was not due to

differential exposure to a foodstuff prior and post freezing.

Campylobacteriosis is more common in males than females up to about age 20 years [9], but the male/ female incidence ratio is about unity in older patients. This age-stratified change in the gender incidence ratio has been attributed to child-to-mother transmission [10]. In the dataset there were 11 groups which involved both an adult and a child aged <16 years with reporting dates more than 1 week apart. In seven of these, the child's infection was reported first, and six of the seven the adults were female. These trends are not statistically significant (binomial distribution P = 0.06) and the one outbreak (outbreak no. 13) where MLST typing data are available shows different sequence types. Therefore further analyses based on larger datasets are needed for evaluating the contribution of child-to-mother transmission to the higher infection rates in adult females.

This study demonstrates that putative household outbreaks of *Campylobacter* in Scotland occurred at a similar incidence as previously found in Wales and Denmark, that household cases are much more common than general outbreaks and that ST strain composition can provide evidence that cases from such outbreaks are epidemiologically related.

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DECLARATION OF INTEREST

None.

REFERENCES

- 1. **Blaser MJ.** Epidemiologic and clinical features of *Campylobacter jejuni* infections. *Journal of Infectious Diseases* 1997; **176** (Suppl. 2): S103–105.
- Ethelberg S, et al. Household outbreaks among cultureconfirmed cases of bacterial gastrointestinal disease. American Journal of Epidemiology 2004; 159: 406–412.
- 3. **Ribeiro CD, Frost JA.** Family clusters of campylobacter infection. *Communicable Disease and Public Health* 2000; **3**: 274–276.

- 4. Forbes KJ, *et al.* Campylobacter immunity and coinfection following a large outbreak in a farming community. *Journal of Clinical Microbiology* 2009; **47**: 111–116.
- Dingle KE, et al. Sequence typing and comparison of population biology of Campylobacter coli and Campylobacter jejuni. Journal of Clinical Microbiology 2005; 43: 340–347.
- Sheppard SK, et al. Campylobacter genotyping to determine the source of human infection. Clinical Infectious Diseases 2009; 48: 1072–1078.
- 7. Manly BFJ. Randomization, Bootsrap and Monte Carlo Methods in Biology, 3rd edn. Boca Raton, Florida, USA: Chapman & Hall/CRC, 2007.
- Anon. Estimates for households and dwellings in Scotland, 2007. 2008, pp. 1–36 (http://www.gro-scotland.gov.uk/statistics/publications-and-data/house hold-estimates-statistics/estimates-of-households-and-dwellings-in-scotland-2007/index.html). Accessed 25 April 2010.
- Strachan NJ, et al. Sexual dimorphism in campylobacteriosis. Epidemiology and Infection 2008; 136: 1492–1495.
- Gillespie IA, et al. Demographic determinants for Campylobacter infection in England and Wales: implications for future epidemiological studies. Epidemiology and Infection 2008; 136: 1717–1725.