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The changing epidemiology of cryptosporidiosis in North West England

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SUMMARY

Between 1996 and 2000, rates of cryptosporidiosis in North West England were significantly higher than overall in England and Wales, particularly during the first half of each year. In addition, during the second quarter of each year in this period, up to 40% of all cases recorded in England and Wales were from the North West Region. In 2001, cryptosporidiosis dramatically decreased throughout the United Kingdom and the springtime excess of cases formerly seen in the North West was no longer apparent. This changed epidemiology was due to a decline in cases of *Cryptosporidium parvum* (formerly genotype 2), associated with zoonotic transmission. Although the initial loss of a spring peak of infection corresponded with the outbreak of foot-and-mouth disease throughout the United Kingdom, its continued absence relates to major structural changes in the North West public water supply. This study highlights the far-reaching public health benefit of local working relationships in addressing re-occurring disease issues.

INTRODUCTION

Transmission of the protozoan parasite *Cryptosporidium* to humans has been documented by direct faecal–oral contact and through drinking water, recreational water and contaminated food and the potential also exists for mechanical transmission via transport hosts such as flies or even birds [1, 2]. In a study of waterborne outbreaks of infectious intestinal disease in England and Wales, *Cryptosporidium* was implicated in all outbreaks associated with public water supplies and public swimming pools [3]. These outbreaks largely involved unboiled chlorinated tap water or chlorinated swimming-pool water and demonstrate that *Cryptosporidium* oocysts can survive some water purification processes.

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In the past 10 years, there have been several springtime clusters of cryptosporidiosis in the United Kingdom relating to various sources of drinking water [4–7]. In one outbreak in North West England, oocysts of *Cryptosporidium* were isolated from Thirlmere reservoir, which supplied the public drinking water distribution system, and from sheep grazing nearby [8], while faecal contamination of water supplies by livestock has been implicated in other outbreaks [9, 10]. A case-control study in North Cumbria also identified drinking unboiled tap water from a public water supply as a significant risk factor for non-outbreak cases of cryptosporidiosis [11].

Human cases of cryptosporidiosis in England and Wales are seasonal with peaks both in spring and autumn [12]. Similar seasonal patterns have been reported in Spain [13] and New Zealand [14]. Cryptosporidiosis in England and Wales is also associated with foreign travel and this is likely to have a seasonal component [15].

Most cases of human cryptosporidiosis have been attributed to *Cryptosporidium parvum* [16]. This parasite has been described in a wide range of wild and domestic mammals [1]. Two cycles of transmission were proposed in 1984, one zoonotic and the other person to person [17] and subsequent development of molecular typing for *Cryptosporidium* has supported this [18, 19], prompting a taxonomic re-evaluation of *C. parvum*. Genotype 1 isolates are almost exclusively limited to humans and have now been classified as a separate species, *C. hominis*, whereas genotype 2 has been isolated from humans and animals and maintains the name *C. parvum* [20]. Genotyping can be used to indicate the likely source of infection for individual cases [21]. A large study of isolates from England showed that all samples from livestock (cows and sheep) were genotype 2 (*C. parvum*) and the proportion of *C. hominis* to *C. parvum* isolates in humans depended upon the time of year of infection, with *C. parvum* predominating in spring [22]. Cryptosporidiosis in sheep shows a strong peak in spring and infection in cattle shows a similar bimodal seasonality to humans [23].

METHODS

Data presented were obtained by the Health Protection Agency Regional Epidemiology Service (North West Regional Office) through the electronic reporting of *Cryptosporidium* isolates in hospital microbiology laboratories in England and Wales (CoSurv). Data received are de-duplicated at the national Communicable Disease Surveillance Centre in London. A subset of about half of reported isolates of *Cryptosporidium* is routinely genotyped by the UK Cryptosporidium Reference Unit in Swansea according to published methods [24] as part of the on-going National Collection of *Cryptosporidium* oocysts [25].

Cryptosporidium oocysts were identified in public water supplies by a standard procedure of filtration and enumeration according to Government legislation [26].

RESULTS

Epidemiology

Between 1996 and 2000, the modest bimodal pattern of seasonality of all *Cryptosporidium* infection in England and Wales became more pronounced,

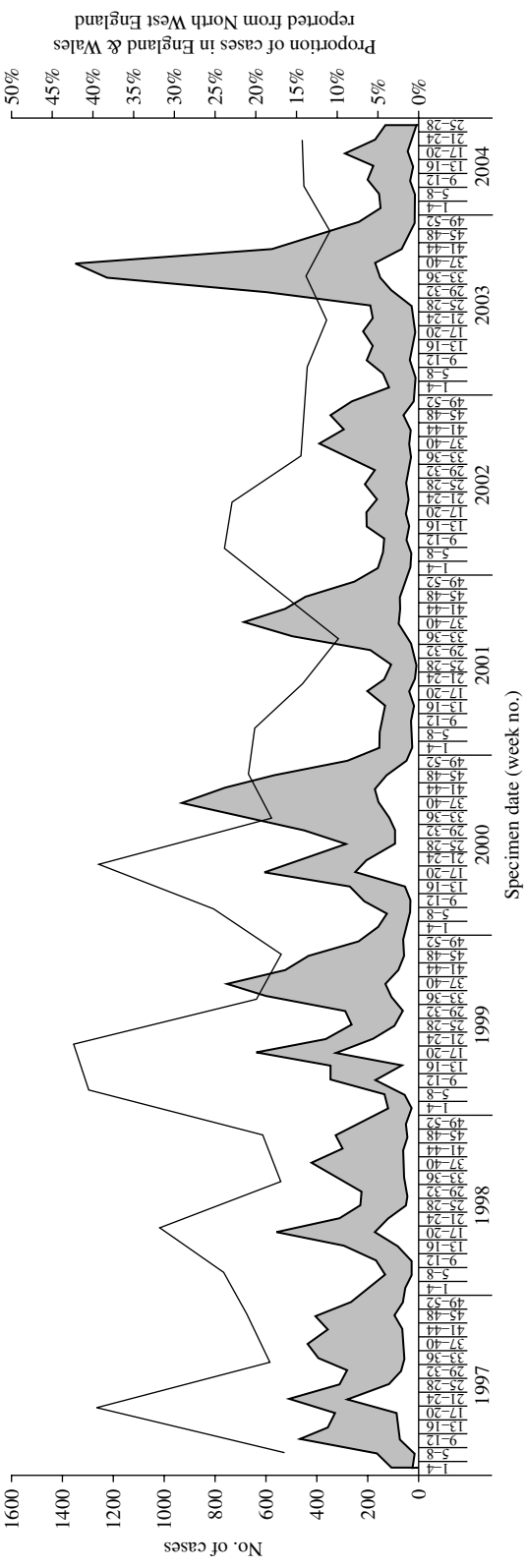

Fig. 1. Laboratory reports of cryptosporidiosis in England and Wales and in North West England between 1997 and 2004, by 4-week period. The line signifies the proportion of cases in England and Wales reported from the North West, by quarter (secondary *x*-axis not shown). ■, Total cases England and Wales; □, North West cases.

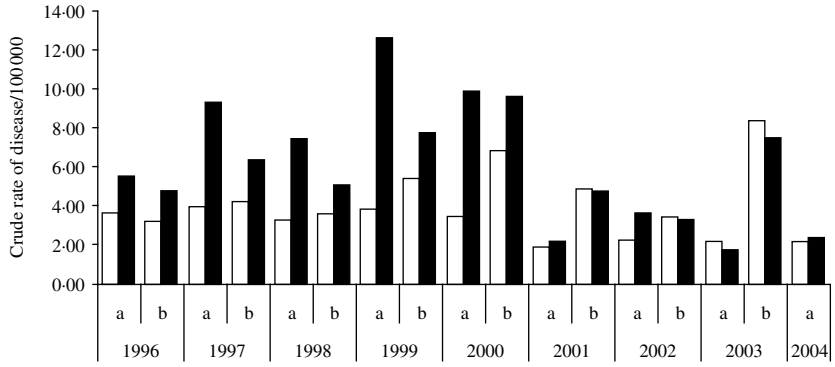

Fig. 2. Crude rates of cryptosporidiosis in England and Wales (□) compared with North West England (■), 1996–2004 by 6-month period (a = weeks 1–26; b = weeks 27–52). Rates are cases per 100 000 population.

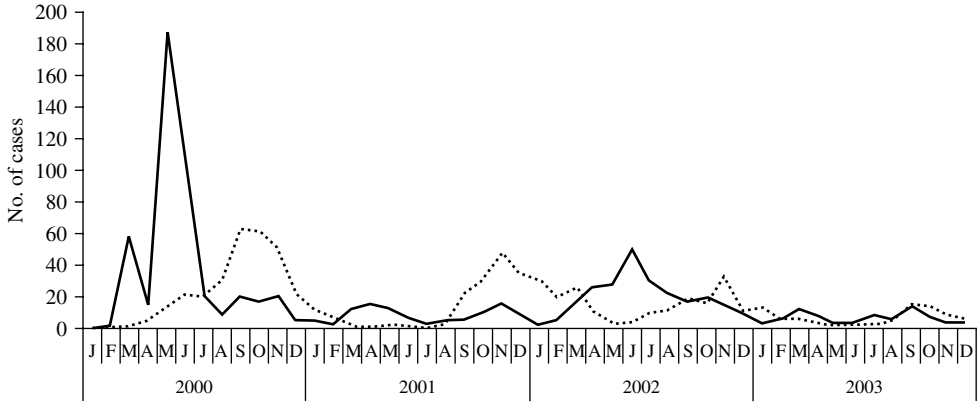

Fig. 3. Number of cases of cryptosporidiosis due to *Cryptosporidium parvum* (——) and *Cryptosporidium hominis* (·····) amongst isolates tested from North West England between 2000 and 2003, by month.

peaking in 2000 with 610 and 938 cases occurring in two distinct 4-week periods around early May and late September respectively (Fig. 1). The seasonal pattern changed significantly in 2001 with the diminishing of the late spring peak, which was not seen in England and Wales subsequently between 2002 and 2004 (Fig. 1). In the North West Region of England, a similar early May peak of infection was seen between 1997 and 2000 but the corresponding September peaks were less pronounced than in England and Wales as a whole (Fig. 1). As in England and Wales, the expected May peak of infection was not seen in North West England between 2001 and 2004.

To assess the contribution made by regional cases to the seasonality in England and Wales, we calculated the proportion of total cases reported by laboratories in the North West each quarter (13-week period) between 1996 and week 28 of 2004 (Fig. 1). The population of the North West Region is about 13% of the population in England and Wales but during the period 1997–2000, between 31 and 42% of all cases reported in England and Wales during the second quarter of each year were from the North West Region (Fig. 1). This increase also diminished in 2001 and although there has been some seasonal variation in subsequent years, it has been less pronounced (Fig. 1).

Analysis revealed that increased rates of infection were seen in the North West Region compared to England and Wales between 1996 and 2000 (Fig. 2). In addition, rates of infection in the North West Region were consistently higher in the first 6 months of the year than in the second where rates in England and Wales as a whole were about equal (except in 2000). Both the seasonality of rates in the North West Region and the increased rates compared with England and Wales were not apparent between 2001 and 2004 (Fig. 2). This pattern was also seen in analysis of rates in separate age groups, suggesting that no particular age group was proportionally more represented than expected in the spring peaks of infection in the North West Region (data not

shown). Likewise, the decrease in rates in 2001 was consistent in magnitude in all age groups analysed, with no age group being proportionately more affected than others (data not shown).

Molecular epidemiology

Genotyping of cases from the North West Region, excluding those with reported overseas travel in the 2 weeks before symptoms, demonstrated that the bimodal seasonality observed in 2000 was defined by separate peaks of *C. parvum* (formerly genotype 2) and *C. hominis* (formerly genotype 1) infection (Fig. 3). Peaks of *C. hominis* cases were still seen in the autumn of 2001, 2002 and 2003, although diminishing in size each year, but spring peaks of *C. parvum* cases were not (Fig. 3) (as already described in the laboratory data). However, there was a doubling in numbers of cases of *C. parvum* infection between May and June in 2002, possibly corresponding to an early summer peak. Analysis of species by age group showed that all age groups analysed were represented in the peaks of *C. hominis* and *C. parvum* described (Fig. 4). The only exception was the rise in *C. parvum* cases in June 2002, which was solely amongst the 15–44 years age group (Fig. 4). These cases were not recorded as part of a recognized outbreak and data available do not show any striking epidemiological links but indicate that, unusually, there were twice as many females as males in this age group.

The sex distribution of cases showed equal proportions of males and females reported from microbiology laboratories between 1996 and 2003. In 2001, 61% of *C. parvum* cases were in males compared with 45% and 46% in 2000 and 2002 respectively (Table 1). Changing sex distribution was also seen amongst *C. hominis* cases where the proportion of males increased from 43% in 2000 to 58% in 2002 (Table 1). In 2003, there were again more male cases of *C. parvum* (56%) and *C. hominis* (51%) although the confidence intervals of these estimates are larger due to the lower number of cases genotyped in 2003.

Geographical distribution

The seasonal variation in numbers of cases was not constant throughout the North West Region. Laboratories in Cheshire and Merseyside reported few cases of *Cryptosporidium* between 1996 and 2004 (to week 26) and there was no clear seasonal pattern. In contrast, data from the counties of Greater Manchester, Lancashire and Cumbria showed strong peaks in early May between 1997 and 2000 (Fig. 5). Peaks of infection in each of these counties were generally limited to the same 4-week period each year, suggesting a seasonally regulated common source of *Cryptosporidium*. The only exception to this pattern was an earlier peak of infection in Lancashire in 1999 (Fig. 5).

The regional decrease in spring cases in 2001 was seen in all county zones of the North West Region but to differing extents. The smallest difference was seen in Cheshire where in 2001, there was a reduction to 35% (12/34) of the average incidence in weeks 1–28 between 1997 and 2000. This time period was chosen to measure only the change in the spring peak of infection and exclude fluctuations in the summer peak. The largest difference in 2001 was seen in Cumbria with a reduction to 13% (12/91) of the average incidence in weeks 1–28 between 1997 and 2000 (Table 2). In 2002, incidence in the first 28 weeks of the year increased in all counties except Cumbria which saw another decrease, but only in Cheshire did incidence reach pre-2001 levels. Subsequent years have shown another decrease in incidence in Greater Manchester and Lancashire and a stabilizing of incidence to $\sim$20% of pre-2001 levels. The spring incidence in Cheshire and Merseyside remains low, but an increasing trend has been evident since 2001 with a rise to above pre-2001 levels in Cheshire and to 85% of pre-2001 levels in Merseyside for 2004 (Table 2).

The impact of changes to the public water supply

In response to the outbreak of cryptosporidiosis linked with elevated levels of oocysts in unfiltered public water supplies in April and May 1999 [8], a number of recommendations were made to the water company serving the region. The outbreak resulted from contamination of Thirlmere-derived supplies, either through contamination of the reservoir itself or by oocysts gaining access to the century-old aqueduct conveying the water to the consumers. At the time of the outbreak, physical treatment was limited to microstraining ($\sim$95 μm pore size) at the head of the aqueduct and there were no further barriers at any of the 16 take-offs along its 150-km length. The long-term solution agreed by the water company was to progressively bypass and close most of these take-offs

Table 1. *The sex distribution of isolates of* Cryptosporidium *genotyped between 2000 and 2003 showing standard errors*

	C. parvum cases				*C. hominis* cases			
Year	Total	Female	Male	S.E.	Total	Female	Male	S.E.
2000	475	55%	45%	2·3%	292	57%	43%	2·9%
2001	101	39%	61%	4·8%	160	47%	53%	3·9%
2002	242	54%	46%	3·2%	193	42%	58%	3·6%
2003	78	44%	56%	5·6%	81	49%	51%	5·6%
Total	896	52%	48%	1·7%	726	50%	50%	1·9%

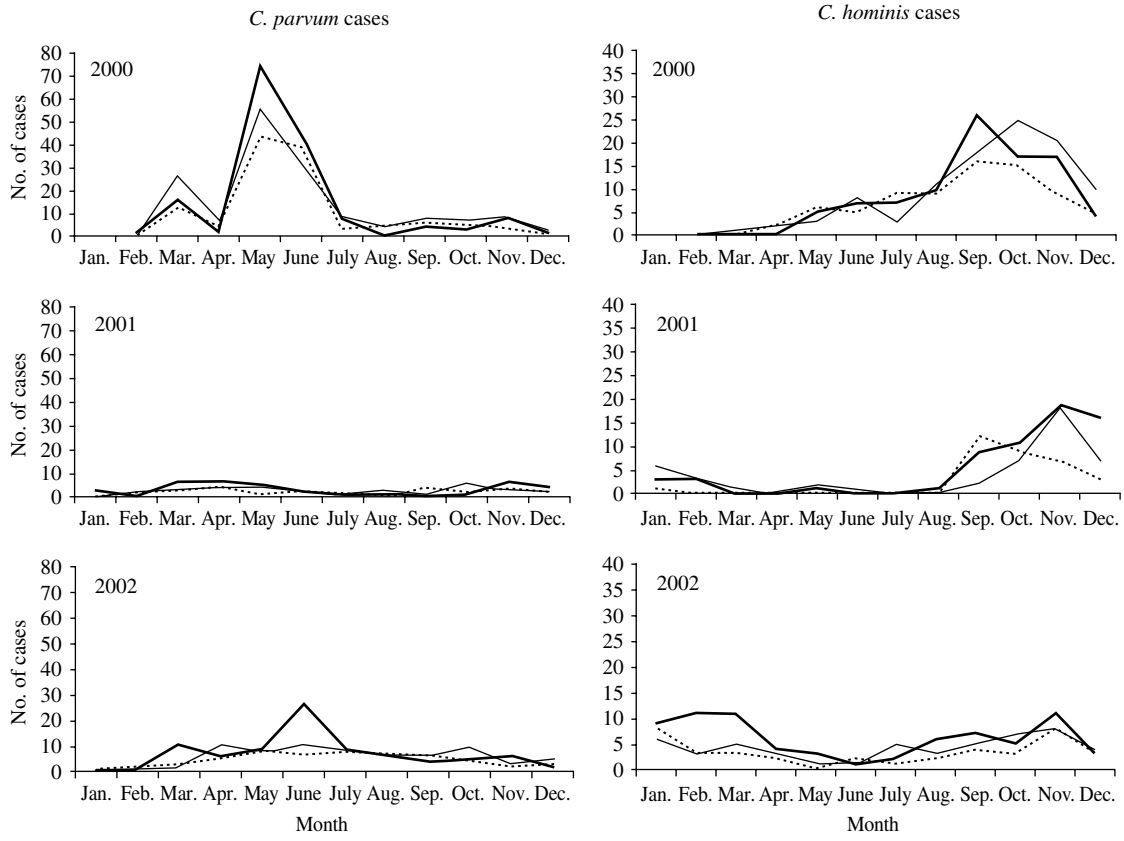

Fig. 4. Age and seasonal distributions of cases of cryptosporidiosis due to *Cryptosporidium parvum* and *Cryptosporidium hominis* amongst isolates tested from North West England between 2000 and 2002, by month. ———, 0–4 years; ——, 5–14 years; ·····, 15–44 years (>45 years old not shown, due to low numbers).

between 2000 and 2004 and upgrade the treatment of any remaining water taken from the aqueduct using coagulation and filtration.

A number of interim measures in and around the Thirlmere supply system were agreed while the long-term work to provide more robust treatment was carried out. These measures aimed to reduce the risk of water becoming faecally contaminated and included removal and restriction of livestock around Thirlmere reservoir and sensitive areas of the aqueduct and improved mixing and dilution of contaminated feeder stream outlets into the reservoir. Continuous monitoring for *Cryptosporidium* oocysts was introduced at the reservoir outlet and aqueduct take-off sites early in 2000, recording a period of increased levels of oocysts between weeks 5 and

Table 2. *Geographical distribution of cryptosporidiosis in North West England 1997–2004* (*weeks 1–28*), *by county*

County	Cases of cryptosporidiosis by year (weeks 1–28)								Average cases 1997–2000 to wk 28	Percentage of 1997–2000 average			
	1997	1998	1999	2000	2001	2002	2003	2004*		in 2001	in 2002	in 2003	in 2004*
Cheshire	32	34	38	32	12	39	28	43	34·0	35	115	82	126
Cumbria	77	91	132	64	12	11	13	29	91·0	13	12	14	32
Lancashire	202	167	254	280	64	81	33	43	225·8	28	36	15	19
Greater Manchester	367	236	474	351	83	157	77	82	357·0	23	44	22	23
Merseyside	8	13	22	9	3	5	8	11	13·0	23	38	62	85
Total	686	541	920	736	174	293	153	208	720·8	24	41	21	29

* Provisional data.

The impact of events in 2001 and subsequent years is measured using the percentage change in numbers of cases (weeks 1–28) compared with the average number during the period 1997–2000 (weeks 1–28). This reference period shows relatively stable trends between counties each year.

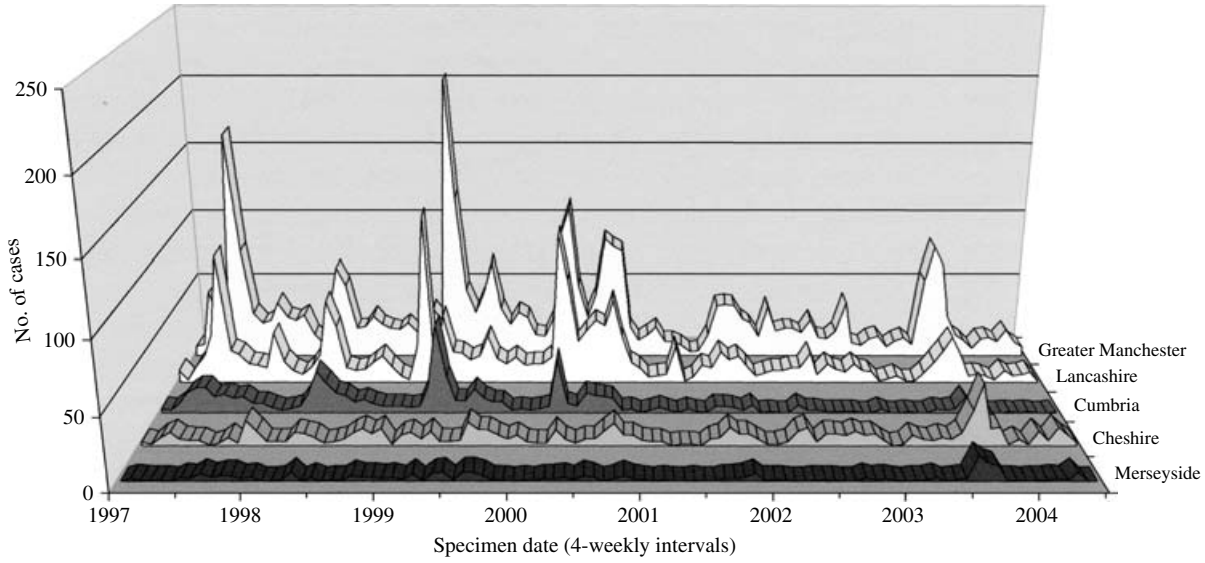

Fig. 5. Laboratory reports of cryptosporidiosis in North West England between 1997 and 2004, by 4-weekly period and by county.

11 (Fig. 6). Over the period of these measures and long-term work (between 2000 and 2004), the mean weekly number of oocysts detected in water taken from all monitored sites showed a consistent annual decline, and no evidence of the spring increase seen in 2000 has been seen in subsequent years (Fig. 6). Work was completed in May 2004.

DISCUSSION

We have described a clear and consistent change in the epidemiology of cryptosporidiosis in North West England and its impact on the infection in England and Wales. Over several years, the incidence of *Cryptosporidium* in the North West Region was disproportionately high, particularly with regard to the late spring peak described in England and Wales [12]. Between 1997 and 2000, 31–42% of cases in England and Wales were reported from the North West Region (April to June), an excess of 18–29% over that expected for the regional population. This was in part due to several annual outbreaks of infection [7, 8] (with the likelihood that previous outbreaks in the region over the past decade were undetected [27]).

The disproportionate contribution of cases from the North West Region may have skewed national data to give the impression of a bimodal seasonality

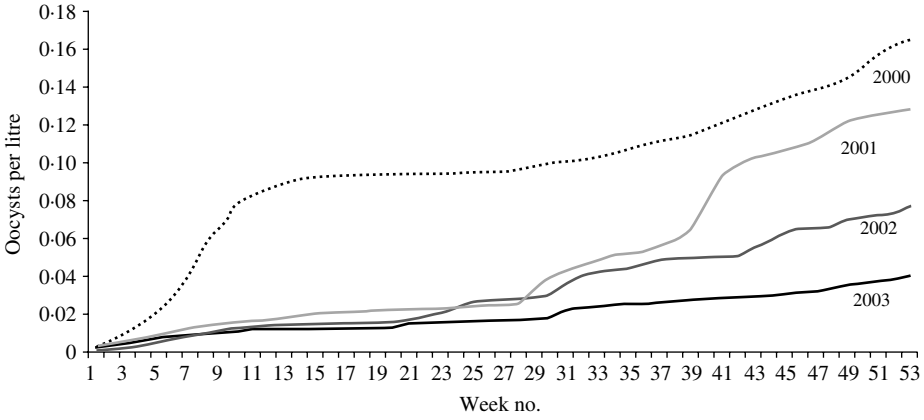

Fig. 6. Cumulative mean weekly number of *Cryptosporidium* oocysts detected in water taken from all monitored sites in the North West between 2000 and 2003.

for the epidemiology of cryptosporidiosis in England and Wales [12]. In fact, many regions in England and Wales only see a rise in incidence during late summer (surveillance data not shown). We explored the reasons for this North West spring peak and its subsequent disappearance in recent years (resulting in the diminishing of a spring peak in England and Wales). Genotyping data indicated that the spring peak was caused by *C. parvum*, the species most often associated with livestock, and the increase in cases may have reflected direct contact with infected animals or indirect contact through contaminated land or water.

The role of the Thirlmere aqueduct in the increased incidence of probable zoonotic infection in spring was described in one outbreak investigation [8] in which a third of cases were between 0 and 5 years old and all those tested were *C. parvum* infections (unpublished outbreak report, Health Protection Agency North West). Investigation of outbreaks in 1997 and 2000 also implicated a possible waterborne source (unpublished outbreak report, Health Protection Agency North West). The likely role of the public water supply in transmission of *C. parvum* (supported here by a spring rise in *C. parvum* incidence in all age groups) prompted the initiation of a major programme of system development in 2000 and it is our belief that these developments have been the key factor in the continuing decreased spring incidence of infection described.

Analysing data over several years allows us to eliminate other explanations for the decrease, in particular those relating to the foot-and-mouth epidemic in the United Kingdom in 2001. The coincident timing of the epidemic with the decrease in spring incidence in 2001 led to speculation that the enforced restriction of contact with animals and the removal of livestock from pasture caused the disappearance of the spring peak of infection [28–30]. Although 47% of all reported cases of foot-and-mouth disease were from the North West of England, there were no instances of foot-and-mouth disease reported from farms within the watershed of the Thirlmere reservoir. Furthermore, restrictions on the movement of animals, brought in to help control the outbreak, ensured that the numbers of sheep on catchment during 2001 remained similar to other years.

Data presented here show a substantial reduction in incidence (at least 65%) in all counties in the North West over the spring period in 2001, indicating a region-wide impact on transmission. The partial recovery described here to pre-2001 incidence levels in 2002 coincides with the 're-opening' of the countryside and supports the suggestion that the countrywide decline in cases of cryptosporidiosis in 2001 was due to restricted access to the countryside contaminated with oocysts [30]. It is almost certain that the epidemic and subsequent countermeasures introduced in the United Kingdom contributed to a decrease in transmission of several livestock-associated zoonoses in 2001 but they cannot account for the continued changed seasonal pattern since 2002 as all countryside restrictions had been lifted by the end of 2001. In addition, a large proportion of the pasture affected by the outbreak in North West England was restocked during 2001.

Another explanation for the decrease in human cases described may be a reflection of lower incidence in livestock following the foot-and-mouth epidemic, as data for Scotland suggests [31]. Although incidence

of cryptosporidiosis in restocked livestock may have been lower initially, another study in the United Kingdom suggests that high and persistent rates of infection in rodents living around farm buildings may be an important driver in infection of reared calves [32]. If this was the case, and prevalence in livestock was the key transmission factor at work for human infection, it might be expected that a year on year recovery of human incidence (as reported in Scotland) would be seen as livestock are systematically re-infected from their environment. This recovery was not shown in data from the North West Region.

Moreover, the levels of incidence in the North West since 2001 have not changed consistently across the counties. In Greater Manchester, Lancashire and Cumbria, where water supplies include a significant contribution from the Thirlmere aqueduct, incidence has remained low whereas the counties supplied from other sources (Cheshire and Merseyside) have shown an increasing trend to pre-2001 levels. Thus, Cheshire and Merseyside counties, where there has never been evidence of seasonal *C. parvum* transmission through the public water supply, could be considered a 'control' for the rest of the region. In the absence of any other intervention apart from the events of 2001, incidence is likely to return to previous levels over a number of years as in Cheshire and Merseyside. The continued lower incidence in spring described here for the other counties suggests that another intervention has been in place in Greater Manchester, Lancashire and Cumbria since 2001.

We have demonstrated that measures taken by the Regional water supplier to improve the treatment of drinking water, in particular through the Thirlmere aqueduct, closely correlate with the decrease in spring incidence of *Cryptosporidium* infection and the presence of oocysts in the drinking water network. Although the role such improvements may have had was initially questioned (because the decline affected the whole of the United Kingdom [29]), we have shown that the disproportionately high incidence of *Cryptosporidium* in North West England during the first half of each year between 1996 and 2000 has disappeared. This implies that whatever the source for 'excess' cases in North West England was before 2001, it is no longer in existence. The most plausible reason for this is the improvement in water quality from the Thirlmere aqueduct. We believe this demonstrates the public health benefit of close cooperation between the public health community and the water industry to identify transmission pathways of key infections and deliver appropriate solutions.

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Some of the data reported in this paper were presented orally at the Health Protection Agency Annual Scientific Conference (2004) and in part in an in-house surveillance report in 2002 (available online ay http://www.hpa-nw.org.uk). Keith Osborn is in the full-time employment of United Utilities, the water company serving North West England, as Public Health Scientist.

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