Effects of weather and river flow on cryptosporidiosis

Iain R. Lake, Graham Bentham, R. Sari Kovats and Gordon L. Nichols

ABSTRACT

Outbreaks of cryptosporidiosis have been linked to weather patterns such as heavy precipitation. However, outbreaks only account for a small percentage of all cryptosporidiosis cases and so the causes of the majority of cases are uncertain. This study assessed the role of environmental factors in all cases of cryptosporidiosis by using ordinary least-squares regression to examine the relationship between the monthly cryptosporidiosis rate, and the weather and river flows in England and Wales between 1989 and 1996. Between April and July the cryptosporidiosis rate was positively related to maximum river flow in the current month. Between August and November cryptosporidiosis was also positively linked to maximum river flows in the current month but only after accounting for the previous month's temperature, precipitation and monthly cryptosporidiosis rate. No associations were found between December and March.

Through an understanding of the environmental processes at work, these relationships are all consistent with an animal to human transmission pathway especially as the relationships vary throughout the year. This study therefore indicates the importance of an animal to human transmission pathway for all cases of cryptosporidiosis.

Key words | cryptosporidiosis, *Cryptosporidium*, environment and public health, greenhouse effect, weather

Iain R. Lake (corresponding author)
Graham Bentham
School of Environmental Sciences,
University of East Anglia,
Norwich NR4 7TJ,
UK
Tel: 01603-593744
Fax: 01603-591327
E-mail: *i.lake@uea.ac.uk*

R. Sari Kovats
Public and Environmental Health Research Unit,
London School of Hygiene and Tropical Medicine,
Keppel St, London WC1E 7HT,
UK

Gordon L. Nichols
Health Protection Agency Centre for Infections,
61 Colindale Avenue, London NW9 5EQ,
UK

INTRODUCTION

Cryptosporidiosis is caused by the protozoan pathogen *Cryptosporidium*. Infected individuals have symptoms of gastro-enteritis which typically last from several days to several weeks, and in immune-compromised individuals, such as those with HIV, the disease can be fatal (Hunter & Nichols 2002). Worldwide cryptosporidiosis is widespread in many developed and developing countries (Hunter 2003) and was responsible for one of the largest waterborne outbreaks ever described in Milwaukee, USA, when over 400,000 people were allegedly infected (Lisle & Rose 1995). Seroepidemiological studies have detected anti-*Cryptosporidium* antibodies in 15 to 44% of the population in developed countries and more than 50% in developing countries (de Graaf *et al.* 1999), indicating that large numbers of the population have been exposed to *Cryptosporidium*.

In England and Wales cryptosporidiosis is also a significant cause of gastro-enteritis and approximately 4,500 notified cases are reported each year (Public Health Laboratory Service 2001). However, recent studies have demonstrated high levels of under-reporting for episodes of diarrhoea (Wheeler *et al.* 1999) and therefore the actual incidence is likely to be closer to 42,000 cases per year (Adak *et al.* 2002).

People become infected with *Cryptosporidium* through animal to human (Casemore *et al.* 1997; Pell 1997) and human to human transmission (Juranek 1995; Casemore *et al.* 1997), including via swimming pools (Dadswell 1996; Rose *et al.* 1997), and infected food and drink (Casemore *et al.* 1997; Nichols 2000). Studies of outbreaks (increases in cryptosporidiosis incidence investigated by public health officials) have demonstrated the importance of weather events (heavy precipitation and high river flows) in transmission through public and private water supplies (Lisle & Rose 1995; Curriero *et al.* 2001). However, in England and Wales around 92% of all

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cases of cryptosporidiosis are not associated with a particular outbreak (Nichols & McLauchlin 2003) and so the causes of most cases are still uncertain. This study assesses the role of environmental factors in all (sporadic and outbreak related) reported cases of cryptosporidiosis by examining the association between the monthly cryptosporidiosis rate, weather, and river flows in England and Wales.

ENVIRONMENTAL SOURCES AND PATHWAYS OF TRANSMISSION

Cattle and sheep are a significant source of *Cryptosporidium* for humans (Casemore *et al.* 1997; Sischo *et al.* 2000). Young animals are especially infectious, with infectivity declining with age as they develop immunity (Sischo *et al.* 2000).

Transmission occurs through oocysts that are shed by the infected animal and once in manure it has been demonstrated that a high percentage of the oocysts can survive for over half a year (Robertson *et al.* 1992). From application to the land, the oocysts may be transferred into rivers but in order for this mobilisation to occur there need to be specific climatic and soil conditions, such as high precipitation falling onto saturated soils. Research has suggested that the leaching and runoff of *Cryptosporidium* from animal manures is a significant process by which *Cryptosporidium* can enter river water (Graczyk *et al.* 2000). This is strengthened by recent genetic typing studies which have shown that a large proportion of UK cryptosporidiosis cases are caused by the animal genotype (McLaughlin *et al.* 2000), suggesting an animal manure source.

Sewage effluent has also been recognised as a source of *Cryptosporidium* in rivers by a variety of authors (Graczyk *et al.* 2000; Roquet *et al.* 2000) and in the UK 40% of all *Cryptosporidium* cases may be sewage-related (McLaughlin *et al.* 2000). Once the *Cryptosporidium* has been washed into rivers the cool and moist conditions are ideal for its survival. However, the oocysts may not simply remain suspended in the water column but can pass into river sediments (Roquet *et al.* 2000) where they can survive for extended periods (Robertson *et al.* 1992) and be resuspended at a later stage.

The mechanisms for oocyst mobilisation, sedimentation and resuspension may explain studies reporting peaks in *Cryptosporidium* concentrations coinciding with heavy rainfall events (Casemore *et al.* 1997; Atherholt *et al.* 1998).

Cryptosporidium is removed from potable water supplies by physical treatment (coagulation, sedimentation and filtration (Rose *et al.* 1997)); thus outbreaks linked to drinking water usually result from a breakdown in the water treatment processes or an absence of adequate treatment (Lisle & Rose 1995).

DATA AND METHODS

The monthly totals of laboratory confirmed cases of cryptosporidiosis reported to the Communicable Disease Surveillance Centre between 1989 and 1996 were obtained. These consist of just over 54,000 cases of cryptosporidiosis of which 1,999 cases (3.7%) were excluded as the individual had reported recent foreign travel indicating that the infection may have been acquired abroad. For each case a date was determined based upon when the stool specimen was taken. The symptoms of cryptosporidiosis usually commence about a week after infection occurs (Arrowroot 1997).

Over the study period Figure 1 indicates that, apart from a large number of cases in 1989, there was no evidence of an annual time trend and so the data were not detrended. However, in order to ensure that our results were not driven by high cases of cryptosporidiosis in this year we examined the impact of controlling for 1989 by including a dummy variable for all the months in 1989 in our analysis.

Cases of cryptosporidiosis exhibit a distinct seasonality and Figure 2 indicates a peak in April, a summer decline and a large autumn peak. The standard deviation bars on the graph indicate that there was a large year-to-year

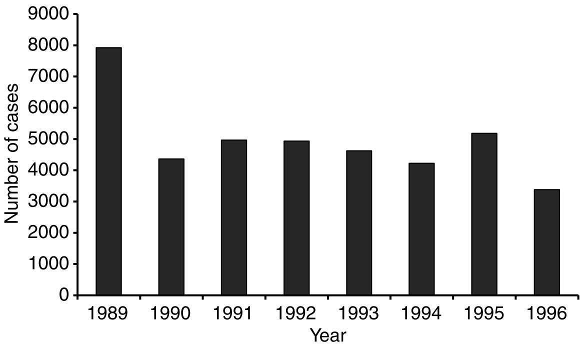

Figure 1 | Number of cases of cryptosporidiosis per year, 1989–1996.

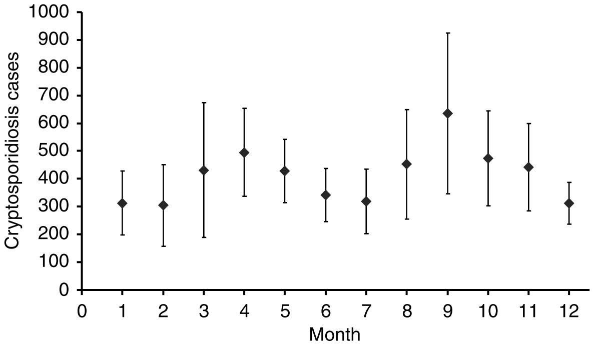

Figure 2 | Mean cases of cryptosporidiosis by month, 1989–1996.

variability in monthly reported cases and our study tests the hypothesis that this is associated with variability in precipitation, temperature and river flow. In order to test this hypothesis we obtained the following information:

The mean temperature for each month was obtained from the British Atmospheric Data Centre. Specifically we utilised the Central England Temperature (CET) series which is a weighted mean temperature for England and Wales derived from measurements at four representative meteorological stations within the area of central England. These data are known to give a good representation of national average conditions (Parker *et al.* 1992).

Monthly precipitation data were obtained from UK Meteorological Office data. These consist of a monthly precipitation total which is an average of the precipitation readings from 35 rain gauges spread evenly throughout the five regions of England and Wales (Jones & Conway 1997).

To provide an estimate of national river conditions the maximum daily flow per month was obtained for each of the three major rivers in England and Wales: the Thames, the Severn and the Trent. Maximum flow was chosen, as this is most likely to correlate with runoff events. These data were obtained from the National Water Archive and the three maximum daily flows per month were averaged to produce one national estimate.

The monthly cases of cryptosporidiosis were divided by the number of days in each month to obtain a monthly rate of cryptosporidiosis.

Because the association between the monthly cryptosporidiosis rate and the environmental variables may vary at different times of the year, the data were analysed by taking each month in turn and using ordinary least-squares regression to examine the relationship between the monthly cryptosporidiosis rate and the temperature, precipitation and river flow in that month.

To account for possible lagged relationships with precipitation, temperature or river events, variables were constructed indicating the values for the three previous months, and average cumulative values across this period. These were then tested in the model. Three months was selected because it is unlikely that a case of cryptosporidiosis will be affected by weather events before this period.

In common with many time series studies it is not possible to assume that the monthly cryptosporidiosis rates are independent in time (i.e. not correlated with the previous month's rate) and therefore an auto-regressive term was included in the model; specifically the cryptosporidiosis rate in the previous month.

Results for individual months were then combined based on those with similar seasonal patterns and statistical results. This has the additional advantage of increasing the degrees of freedom and consequently the statistical robustness of the results. This procedure derived three time periods, April to July, August to November, and December to March. When the data from individual months are combined it became important to control for seasonality and so all models were analysed incorporating dummy variables for each of the individual months.

RESULTS

The results of the ordinary least-squares regression demonstrated that in the period April to July the monthly cryptosporidiosis rate was strongly associated with the maximum river flow that month (Figure 3). Temperature and precipitation were not significant in the model and neither were any of the lagged independent variables. This model is presented in Table 1. When variables were added into the model to control for autocorrelation (the previous monthly cryptosporidiosis rate) and seasonality (dummy variables for each individual month) the maximum river flow that month remained highly significant with a similar parameter estimate. A similar result was observed when a dummy variable was inserted for the months during 1989,

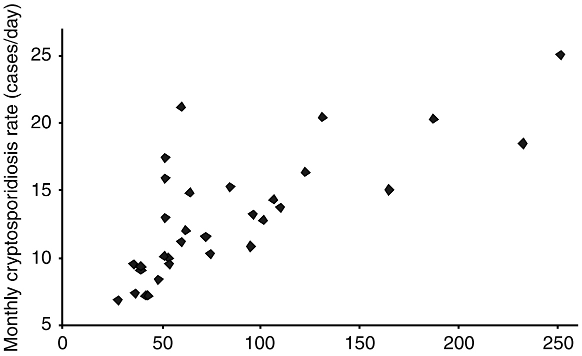

Figure 3 | Monthly cryptosporidiosis rate and maximum river flow between April and July.

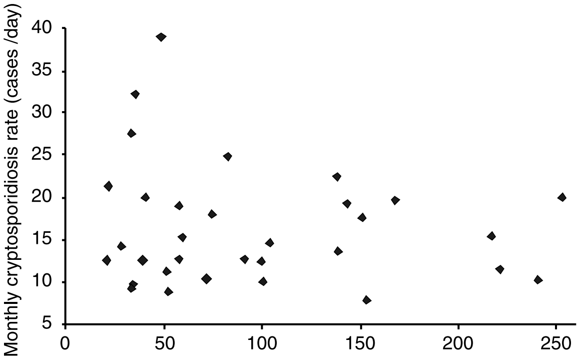

Figure 4 | Monthly cryptosporidiosis rate and maximum river flow between August and November.

indicating that the result was not driven by the high numbers of cryptosporidiosis cases that year.

During the period August to November a model including maximum river flow as the only explanatory variable indicated no association with the monthly cryptosporidiosis rate (Figure 4). When the autocorrelation term was entered into the model it was highly significant but the maximum river flow was still not significant. It was only when temperature and precipitation in the previous month were included in the model that the maximum river flow became highly significant. This model is presented in Table 2 and the result was stable when seasonality was accounted for by inserting dummy variables for each individual month into the model. It was also stable when a dummy variable was inserted for all the months in 1989.

Between December and March no significant associations were observed.

Table 1 | Ordinary least-squares regression model of monthly cryptosporidiosis rate and maximum river flow between April and July

Variable	Estimate[a]	95% CI	t-value
Intercept	7.85***	5.90–9.81	7.86
Current month's maximum river flow (m^3 s^{-1})	0.0614***	0.0420–0.0809	6.20

r^2 54.7%
Degrees of freedom 31
*$p < 0.05$, ** $p < 0.01$, *** $p < 0.001$
[a] The change in monthly cryptosporidiosis rate per unit change in the explanatory variable

DISCUSSION AND CONCLUSIONS

Our results are consistent with the hypothesis that weather plays a significant role in the seasonal pattern of cryptosporidiosis. From April to July, and especially during the early part of this time period, the increase in cryptosporidiosis may be due to the release of large numbers of newborn, and hence highly infectious, animals onto the land. At this time the land is usually saturated with water so any excrement and its accompanying *Cryptosporidium* is readily washed into watercourses, hence the strong link to the current month's maximum river flow. This is supported by recent genetic typing work suggesting that the majority of cryptosporidiosis cases in the early part of the summer are infected with genotype 2 indicating a livestock source (Nichols & McLauchlin 2003). The association with river flow may also be driven by the resuspension of *Cryptosporidium* from river sediments.

Between August and November the monthly cryptosporidiosis rate is not significantly associated with maximum river flow. This variable only becomes significant once autocorrelation, and temperature and precipitation in the previous month have been accounted for, indicating that a less straightforward mechanism is at work. The importance of the autocorrelation term in the model suggests that secondary infections are of greater importance at this time of year. This is supported by results from genetic typing work suggesting that a large number of cryptosporidiosis cases in late summer and early autumn are caused by genotype 1 suggesting a human sewage source to the infection (Nichols & McLauchlin 2003).

Table 2 | Ordinary least-squares regression model of monthly cryptosporidiosis rate and the autocorrelation term, the previous month's precipitation and temperature and the maximum monthly river flow, between August and November

Variable	Estimate[a]	95% CI	t-value
Intercept	-27.6^{**}	$-44.5 - -10.8$	-3.21
Previous month's cryptosporidiosis rate	0.757^{***}	$0.559-0.956$	7.47
Previous month's precipitation (mm)	-0.00785^{*}	$-0.0135 - -0.00218$	-2.71
Previous month's temperature (°C)	2.09^{***}	$1.24-2.93$	4.85
Current month's maximum river flow ($m^3\,s^{-1}$)	0.0819^{***}	$0.0445-0.119$	4.29

r^2 68.8%
Degrees of freedom 31
$^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$
[a] The change in monthly cryptosporidiosis rate per unit change in the explanatory variable

However, there is still evidence of animal to human transfer in the August to November period as monthly cryptosporidiosis rates are positively associated with temperature in the previous month but negatively associated with precipitation in the previous month. Together these associations imply that the monthly cryptosporidiosis rate is higher if the previous month is warm and relatively dry. Warm dry weather is associated with times when the soil moisture deficit is likely to be high and hence any *Cryptosporidium* falling onto the land is likely to build up on the fields and not be transferred to watercourses. Only when temperature and precipitation have been included in the model is the month's maximum river discharge significant, implying that runoff is occurring and washing this build-up of *Cryptosporidium* into watercourses.

In the winter months, between December and March, many animals are housed indoors. This factor, combined with high precipitation, which would minimise the build up of *Cryptosporidium* from any livestock which are on the land, is likely to lead to low *Cryptosporidium* concentrations in surface waters. Therefore, we would not expect cryptosporidiosis cases to be linked to weather events.

This paper has shown associations between all (sporadic and outbreak) cases of cryptosporidiosis and weather. The high explanatory power of the models combined with the observation that most cases are not outbreak related lead us to hypothesise that, in addition to outbreaks (Lisle & Rose 1995; Curriero *et al.* 2001), contaminated drinking water may be a significant source of sporadic cryptosporidiosis cases in England and Wales.

A limitation of the study is that it was conducted at a national level averaging the large variations in weather and agriculture that occur across the country. This may be a particular problem in the summer when weather events can be very localised. Another limitation is that the observed association with environmental conditions may be the result of confounding by other factors not taken into account in this study. However, we have taken seasonal confounding into account as far as possible by looking at months separately and incorporating dummy variables of individual months into the ordinary least-squares regression models. Within these time periods we are not aware of any aetiological factors that would be strongly associated with the observed relationships with weather and river flow, so confounding does not seem likely.

Global climate change will affect precipitation and temperature in the UK. Increases in temperature will lead to animals being released onto the fields earlier in the year possibly bringing forward the onset of the *Cryptosporidium* peak, which currently occurs in April. Summers and springs will be drier in the south-east and wetter in the north-west (Hulme & Jenkins 1998) and all areas are likely to see increased precipitation in the autumn and winter. In the south-east this may decrease the numbers of cases between

April and July, but drier summers coupled with wetter autumns may increases cases in the autumn. The opposite pattern may be observed in the north-west with more cases in the spring and early summer due to higher precipitation, and wetter summers and autumns leading to less build-up of *Cryptosporidium* in the environment possibly lowering cases of cryptosporidiosis in the August to November period. Our results indicate that higher winter precipitation is unlikely to have an impact on cases of cryptosporidiosis.

However, these projected changes may be offset by the new legislation on *Cryptosporidium* in public water supplies, together with substantial increases in infrastructure investment by the water industry.

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