A Cryptosporidium hominis outbreak in North-West Wales associated with low oocyst counts in treated drinking water
B. W. Mason, R. M. Chalmers, D. Carnicer-Pont and D. P. Casemore

ABSTRACT
An outbreak in the autumn of 2005 resulted in 218 confirmed cases of Cryptosporidium hominis. The attack rate (relative risk 4.1, 95%CI 2.8–9.1) was significantly higher in the population supplied by Cwellyn Water Treatment Works (WTW). A case–control study demonstrated a statistically significant association (odds ratio 6.1, 95% CI 1.8–23.8) between drinking unboiled tap water and C. hominis infection. The association remained significant in a logistic regression analysis, with an adjusted odds ratio of 1.30 (95 CI 1.05–1.61) per glass of unboiled tap water consumed per day. This evidence together with environmental and associated microbiological investigations, and the absence of effective treatment to remove Cryptosporidium oocysts at the WTW, led to the conclusion that the outbreak was waterborne. Oocyst counts in final treated water at the WTW and at different points in the distribution system were consistently very low, maximum count in continuous monitoring 0.08 oocysts per 10 litres. Data from continuous monitoring and the epidemic curve is consistent with the hypothesis that low numbers of oocysts of C hominis were present in treated water continuously during the outbreak and these were of sufficient infectivity to cause illness. All surface water derived water supplies present a potential risk to human health and appropriate control measures should be in place to minimise these risks.

Key words | case–control study, Cryptosporidium hominis, low oocyst counts, molecular methods, outbreak management, waterborne outbreak

INTRODUCTION
An outbreak of cryptosporidiosis occurred in North West Wales in the later part of 2005. Two hundred and thirty-one laboratory-confirmed cases of cryptosporidiosis were notified between 1st October 2005 and 31st January 2006 in residents of two neighbouring local authorities, Gwynedd and Anglesey. Two hundred and eighteen of these cases were confirmed as Cryptosporidium hominis infection by the UK Cryptosporidium Reference Unit (CRU). In comparison 36 laboratory-confirmed cases of cryptosporidiosis were identified in this population during the whole of 2004. The possibility of an outbreak was identified during the first week of November 2005 as a result of a cumulative total of 21 notifications since the beginning of September, together with a marked increase in the number notified in the week commencing 31st October, which eventually totalled 15 during that week. An incident management team (IMT) was set up on 7th November to initiate investigation. Preliminary descriptive epidemiological findings suggested a possible link with the drinking water supply derived from a reservoir, Llyn Cwellyn, operated by Dwr Cymru/Welsh Water (DCWW). The lake is situated at the foot of Mount Snowdon in the Snowdonia National Park. The treated supply serves a population of approximately 60,000. There is a small village, Rhyd Ddu, approximate resident population 200, at the head of the lake. The area also receives large numbers of tourists throughout the year.

Following a site visit by members of the IMT, a precautionary reminder for severely immunocompromised patients to boil their water was issued to clinicians on 18th November.

We report the results of the epidemiological investigations which identified water obtained from Llyn Cwellyn as the most likely source of the outbreak and review the cases in the context of the available Cryptosporidium monitoring data. The environmental investigations that also helped to establish the public water supply as the source of the outbreak are described in an accompanying paper (Chalmers et al. 2010).

METHODS

Epidemiology of the outbreak

Symptomatic individuals from whom Cryptosporidium oocysts were detected in faecal samples submitted to local microbiology laboratories were identified as cases and interviewed using a standard questionnaire based on that recommended in sub-appendix A4.1 of the Bouchier Report (1998), by local Environmental Health Officers. The questionnaire collected information on exposures during the two weeks prior to onset which included: travel outside the UK; travel within the UK; food and drink supply and consumption at home and elsewhere (e.g. place of work); source of drinking water; exposure to recreational water; animal exposure; and illness in other members of the household.

Cases were classified as secondary if anyone in the household had a history of diarrhoea (three or more loose stools in 24 hours) in the two weeks prior to onset of symptoms. Information on the normal source of water supplied to the household was obtained from the Water Company for each case. The Water Company also provided estimates of the population normally supplied by each drinking water source.

The attack rates for the population supplied with water from the Cwellyn WTW and the population supplied exclusively from other sources were calculated. The relative risk of Cryptosporidium in the population supplied from Cwellyn was calculated by comparison with the population supplied exclusively from other sources.

Cryptosporidium-positive faecal samples were referred to the CRU for typing to the species level by PCR-RFLP Cryptosporidium oocyst wall protein (COWP) gene (Spano et al. 1997) as described previously (Anon 2002). A sub-set of 71 C. hominis isolates, selected from cases who had not travelled abroad and who had no history of contact with household cases of diarrhoea, was subtyped at the GP60 locus by bi-directional DNA sequence analysis (Alves et al. 2003).

Case–control study

To test the hypothesis that Cryptosporidium infection was associated with the consumption of unboiled tap water a case–control study was undertaken. For the purpose of the case–control study a case was defined as a resident of Gwynedd or Anglesey aged 16 years or older with: diarrhoea (three or more loose stools in 24 hours) with an onset after 1st September; and C. hominis as the only isolate from a faecal specimen. Cases were excluded if they had a history of travel outside the UK or a contact with a household member with a history of diarrhoea, during the two weeks before onset. Potential cases reported by the local laboratory between 3rd October and 20th November were interviewed using a structured outbreak questionnaire based on that recommended in sub-appendix A4.5 of the Bouchier Report (1998), which collected information about a range of exposures in the two weeks before onset of symptoms.

One hundred potential controls were identified by selecting random telephone numbers from the telephone directory for the same area. An individual was eligible to be a control if they: were a resident of Gwynedd or Anglesey aged 16 years or older; and did not have a history of travel outside the UK in the two weeks prior to 5th November, or a household contact with new onset of diarrhoea since 1st September. Controls were interviewed by telephone during the daytime and evening between Monday 14th and Friday 18th November using a structured questionnaire that was equivalent to that used for cases. Controls were asked about exposures in the two weeks before 5th November, chosen since it is “Bonfire Night”, a memorable date in the UK marked by fireworks displays and relevant to the timeframe of the investigation.
Questionnaire data were collated using Epi Info 6.04 (Epidemiology Program Office 2001) and odds ratios, 95% confidence intervals, Fisher’s exact test, chi-squared tests, two-sided t tests, Spearman’s rho and logistic regression were calculated using STATA 10.0 (StataCorp 2007). Step-down multivariate logistic regression was performed using explanatory variables with odds ratios from the univariate analysis with a p value ≤ 0.2. At each stage the variable that made the least contribution to the explained variation was excluded until all remaining variables were significant. Age and the number of glasses of unboiled tap water consumed per day were modelled as continuous variables in the logistic regression.

Water supply and treatment

At the time of the investigation Llyn Cwellyn, was classed as a low risk (category A1) source (Council Directive 1975). The Water Company’s risk assessment in 1999, carried out in compliance with the water quality regulations (Statutory Instrument 1999), accepted this classification and treatment had not been designed or subsequently modified specifically to deal with Cryptosporidium. It was assumed that pollutants entering the lake would receive sufficient dilution in the total volume of water therein. Treatment at the water treatment works (WTW) comprised pressure filtration (aimed primarily at reduction of naturally occurring manganese) and disinfection by chlorination. It was the view of DCWW at the time that the characteristics of the water did not permit the use of coagulation. A small sewage treatment works, also managed by DCWW, serves the village of Rhyd Ddu and discharges into the River Gwerthai, which feeds into the lake at the opposite end to the WTW. Several septic tanks and small-scale sewage treatment plants are located at properties around the lake in areas prone to flooding. A detailed sampling programme was undertaken to investigate the water source and catchment, described in the accompanying paper.

Cryptosporidium monitoring

As a result of an undertaking between DCWW and the Drinking Water Inspectorate (DWI) following previous unrelated water quality problems, continuous monitoring for Cryptosporidium was carried out on Cwellyn final water from 2nd November, using Filta-Max® sampling filters according to the methods defined by the regulatory standard operating protocols (Statutory Instrument 1999); analysis of the samples was carried out by an approved water industry laboratory on behalf of DCWW. Additional continuous filters were also set up at three points on the treated water distribution system. Filter samples were also taken from the final water at Mynydd Llandegai water treatment works which is blended with Cwellyn water at a storage tank at Pentir before going on to supply Bangor and South Anglesey.

RESULTS

Epidemiology of the outbreak

Of the 231 individuals with faecal samples in which Cryptosporidium oocysts were identified by the local laboratory 218 were confirmed as C. hominis. Of the subset of 71 C. hominis isolates that were sub-typed, 63 were subtype IbA10G2 and eight did not amplify with the PCR primers. Onset dates were available for 191 of the confirmed cases and 132 of these were classified as primary infections (Figure 1).

Fifty-six percent (122/218) of cases were female and 44% (96/218) male. The difference is significant (chi squared, p = 0.02). Cases were aged 0 to 92 years, the majority were adults (131 of 218) and 30% (65 of 218) were less than 10 years of age. Female cases (mean 28 years,
median 23 years) were significantly older (t-test, \( p < 0.0001 \)) than male cases (mean 16 years, median 12 years).

The attack rate was significantly higher in the population supplied by Cwellyn Water Treatment Works (Table 1). The relative risk of primary \( C. \) hominis infection in the population supplied by Cwellyn WTW was 4.1 (95% CI, 2.8–6.1, \( p < 0.0001 \)).

Case–control study

Forty-five of the 69 cases eligible at this stage met the study case definition. Forty of the potential controls were contactable and agreed to be interviewed, 37 of whom met the study control definition.

There was no gender difference between cases and controls, 76% of cases and 75% of controls were female. However, controls were significantly older than cases, mean 63 years for controls compared to 39 years for cases (t-test, \( p < 0.001 \)). There was no association in controls between age and the number of glasses of unboiled tap water consumed, correlation coefficient 0.07, \( p = 0.70 \).

Drinking unboiled tap water was significantly associated with disease, odds ratio 6.1, \( p = 0.002 \) (Table 2). No other significant risk factors were found on univariate analysis, although contact with a farm appeared to be protective.

A dose–response relationship was found with an increasing risk of disease with higher consumption of unboiled tap water (Table 3). Age and the number of glasses of unboiled tap water drunk per day were the only significant variables in the logistic regression model (Table 4).

Water supply and treatment

There had been no clearly identifiable adverse event or challenge indicating a plant under strain, as defined by the

<table>
<thead>
<tr>
<th>Source</th>
<th>Cases</th>
<th>Population supplied</th>
<th>Attack rate per 100,000 population</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cwellyn*</td>
<td>118</td>
<td>60,656</td>
<td>195</td>
<td>161–234</td>
</tr>
<tr>
<td>Other</td>
<td>35</td>
<td>74,402</td>
<td>47</td>
<td>33–65</td>
</tr>
<tr>
<td>Total</td>
<td>153</td>
<td>135,058</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Water either solely from Cwellyn or as a blend of Cwellyn and Myndd Llandegai.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Cases (( n = 45 ))</th>
<th>Controls (( n = 37 ))</th>
<th>OR (95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drink bottled water</td>
<td>Exposed 14</td>
<td>Non exposed 31</td>
<td>0.5 (0.2–1.4)</td>
<td>0.18</td>
</tr>
<tr>
<td>Private water supply home</td>
<td>Exposed 0</td>
<td>Non exposed 45</td>
<td>0 (0–1.6)</td>
<td>0.20</td>
</tr>
<tr>
<td>Swimming in a pool</td>
<td>Exposed 5</td>
<td>Non exposed 40</td>
<td>2.2 (0.3–24.1)</td>
<td>0.45</td>
</tr>
<tr>
<td>Drink unboiled tap water*</td>
<td>Exposed 40</td>
<td>Non exposed 5</td>
<td>6.1 (1.8–23.8)</td>
<td>0.002</td>
</tr>
<tr>
<td>Wash fruit or salad</td>
<td>Exposed 41</td>
<td>Non exposed 4</td>
<td>2.0 (0.2–4.4)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Others

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Cases (( n = 45 ))</th>
<th>Controls (( n = 37 ))</th>
<th>OR (95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boating</td>
<td>Exposed 1</td>
<td>Non exposed 44</td>
<td>0.8 (0.01–69)</td>
<td>1.0</td>
</tr>
<tr>
<td>Contact with farm</td>
<td>Exposed 0</td>
<td>Non exposed 45</td>
<td>0 (0–0.3)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Contact with pets</td>
<td>Exposed 24</td>
<td>Non exposed 21</td>
<td>0.6 (0.3–1.5)</td>
<td>0.37</td>
</tr>
<tr>
<td>Fruit juice drink</td>
<td>Exposed 29</td>
<td>Non exposed 6</td>
<td>0.4 (0.2–1.3)</td>
<td>1.0</td>
</tr>
<tr>
<td>Shellfish eating</td>
<td>Exposed 1</td>
<td>Non exposed 42</td>
<td>0.1 (0.01–1.4)</td>
<td>0.09</td>
</tr>
<tr>
<td>Social events</td>
<td>Exposed 11</td>
<td>Non exposed 34</td>
<td>0.8 (0.3–2.3)</td>
<td>0.62</td>
</tr>
<tr>
<td>Travel within UK</td>
<td>Exposed 11</td>
<td>Non exposed 34</td>
<td>3.7 (0.9–22)</td>
<td>0.08</td>
</tr>
<tr>
<td>Contact with child &lt; 5 years old</td>
<td>Exposed 6</td>
<td>Non exposed 39</td>
<td>1.3 (0.3–5.1)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*Any source: Cwellyn or other.
Group of Experts (Badenoch 1995). Neither had any failure of water treatment been identified by the water company. Although oocysts were detected in the supply numbers detected were well below the level indicated in the legislation as unacceptable (1/10 L/1000 L/24 hrs). Although classed as a pristine (A1) source there were a number of potential sources of pollution, including a small sewage treatment works (STW) at the head of the lake which serves the village of Rhyd Ddu. There were at least 13 septic tanks at properties in the catchment. Although not directly relevant to this outbreak investigation there was bank side pasture with livestock grazing. In terms of the risk assessment for the source, it should have indicated a risk of Cryptosporidium contamination. The area was one in which heavy rain was common and the terrain was typically ‘flashy’ permitting rapid spate flows into the lake from water courses and there was a history of intermittent flooding in low-lying areas. Observation of the lake indicated the likelihood of wind-driven streaming. The general topography also suggested the possibility of seasonal thermal stratification. These issues are further explored in the accompanying paper (Chalmers et al. 2010).

There had been a history of intermittent water quality monitoring failures, including the finding of E. coli and Clostridium and periods of high turbidity. Some of the latter were related to soil colloids resulting from forestry work and not effluent pollution but would present a challenge to water treatment. These failures had led to the formal undertaking with DWI, including the setting up of continuous monitoring for Cryptosporidium just prior to the recognition of the outbreak. Occasional 10 L grab samples of the raw water had been taken by DCWW and examined for Cryptosporidium, with negative results. However, the size and frequency of samples was inadequate for a realistic assessment.

The pressure filters were not designed for the removal of Cryptosporidium and their efficiency could not be enhanced by coagulation because of the thin nature of the water. Individual turbidity meters were fitted to each filter and slow start up was used following filter backwashing, in accordance with the Group of Experts (Badenoch 1995). However, the water treatment data records showed a significant increase in turbidity in the start up phase, indicating a period when increased passage of oocysts trapped in the filter matrix might have occurred.

It was thus clear that there were no effective barriers to Cryptosporidium either naturally in the catchment or man-made in terms of water treatment.

### Cryptosporidium monitoring

Continuous sampling for Cryptosporidium took place from early November 2005. Oocyst counts in raw water, final treated water at the water treatment works and at different points in the distribution system were generally consistently very low (Table 5). The average number of oocysts per 10 litres per large volume (≥ 1,000 L) continuous sample in final treated water at the Cwellyn WTW were consistently below the regulatory treatment standard (average of less than one oocyst per 10 litres in a continuous sample at 40 litres/hr/∼24 hrs) specified for sites identified as at significant risk of Cryptosporidium (Figure 2) (Water Quality Regulations 2000/01). However, oocysts were detected frequently, in 56/89 (63%) samples. In addition, two oocysts were detected in a 10 litre grab sample taken by DCWW from the treated water storage tank at Cwellyn WTW on 2nd November. C. hominis was confirmed in a continuous sample from the distribution system on 7th November.

### Table 3 | Dose–response number of glasses of unboiled tap water consumed per day

<table>
<thead>
<tr>
<th>Number of glasses of unboiled tap water consumed</th>
<th>Cases (n = 45)</th>
<th>Controls (n = 37)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>5</td>
<td>16</td>
<td>Ref.</td>
</tr>
<tr>
<td>1 to 4</td>
<td>23</td>
<td>17</td>
<td>4.3 (1.3 – 14.1)</td>
</tr>
<tr>
<td>5 to 8</td>
<td>11</td>
<td>3</td>
<td>11.7 (2.3–59.5)</td>
</tr>
<tr>
<td>More than 8</td>
<td>6</td>
<td>1</td>
<td>19.2 (1.8–199.9)</td>
</tr>
</tbody>
</table>

### Table 4 | Multivariate analysis

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number glasses unboiled tap water consumed per day</td>
<td>1.43 (1.17–1.76)</td>
</tr>
<tr>
<td>Age in years</td>
<td>0.94 (0.92–0.97)</td>
</tr>
</tbody>
</table>
Control of the outbreak

As a result of the outbreak investigation and in the absence of effective water treatment a public advice notice to boil water (BWN) was issued by DCWW on 29th November following a decision by the Outbreak Control Team (OCT). The IMT became an OCT at this point in time. This superseded a request to general practitioners and medical consultants in north-west Wales on 18th November to issue advice on boiling drinking water to patients with impaired T-cell immunity in line with the definition of severely immunocompromised recommended by the Group of Experts (Bouchier 1998). Although the regulations then in force did not permit the use of disinfection rather than removal of oocysts, on the basis of available scientific evidence the Water Company accepted advice to install a UV treatment plant suitable for the purpose (Hanovia®). This was the only effective treatment that could be installed within a reasonable time frame that would permit lifting of the BWN. The BWN was in place for nine weeks until the UV treatment plant had been installed and commissioned at the Cwellyn WTW, and the notice was finally lifted on 30th January 2006.

Following the outbreak, DCWW pleaded guilty to four counts of supplying water unfit for human consumption at Caernarfon Magistrates’ Court on 11th October 2007 under The Water Companies Act (1991). The lessons learned from the outbreak led to major modification of the relevant water quality regulations (Statutory Instruments 2007). It also led
to the setting up in Wales of a new multiagency liaison group, the Water and Health Partnership, to coordinate the approach to any future incidents or outbreaks.

**DISCUSSION**

The case–control study demonstrated a statistically significant association between the consumption of unboiled tap water and *C. hominis* infection. The association is unlikely to be the result of any confounding arising from the age difference between cases and controls as the association and dose–response relationship remained significant in the multivariate logistic regression.

Controls were significantly older than cases. However, there was no association in controls between age and the volume of unboiled tap water consumed. The trend in controls, albeit non-significant, was for consumption of unboiled tap water to increase with age. In general, immunity to *Cryptosporidium* infection also increases with age. The inclusion of a greater proportion of individuals who are immune in the control group, who could not develop disease if exposed to the source of infection, will reduce the size of any association between exposure and disease. Overall the effect of an older control group probably reduced the size of the observed association between the consumption of unboiled tap water and *C. hominis* infection. Given the low numbers of oocysts in the supply and the prolonged period of exposure, some of those cases classed as household contact secondary cases could have been co-primary cases. This mis-classification may have further reduced the apparent strength of association.

Recall bias can occur in case–control studies if there are differences in the way exposure information is remembered or reported by cases who have experienced an undesirable health outcome, and by controls who have not. Recall bias is unlikely to have been particularly important in this study because it was undertaken before any publicity about the outbreak and there had been no history of previous outbreaks in the area. There were 12 cases whose water at home was not supplied from Cwellyn WTW. Eight of them had visited or worked in the area serviced by Cwellyn during the incubation period. The other four cases could either be explained by the background epidemiology of the disease or other factors that we have not identified. This would not affect the outcome of the study.

The response rate in controls was only 40%. It is possible that controls who participated were different from those who did not, which may have led to biases in the result. Information on the controls who did not participate is not available and it is not possible to determine any effects of the low response rate. Low response to telephone surveys is well recognised and the response rates have declined in the UK in the past decade (*Boland et al. 2006*). Younger people are less likely to have a land line (*E-citizen 2005*), and those under 44 are the most difficult to contact in telephone surveys (*Boland et al. 2006*). The case–control study design was based on the guidance on the epidemiological investigation of outbreaks of infection contained in appendix A4 of the *Bouchier Report (1998)*. This guidance recommend that matching is not used and that if frequency matching is used to ensure a roughly even distribution of age between cases and controls age bands of <6 years, 6–15 years and over 15 years are used. Although we believe that the age difference between cases and controls in this study did not invalidate the results, and the only real danger arising from the age difference is that it could have hidden or reduce the size of a real association. Those planning future studies may wish to address this issue in their study design.

The evidence from the case–control study, high attack rate in the population supplied from Cwellyn, environmental and associated microbiological investigations, and the absence of effective treatment to remove *Cryptosporidium* oocysts in the water treatment works, led to the conclusion that the outbreak was waterborne. The evidence meets the highest level criteria for classifying the association of the outbreak with water, i.e. would be classed as strongly associated (*Tillett et al. 1998*).

The outbreak investigation and case–control study were facilitated by the routine local laboratory examination for *Cryptosporidium* of all first-time faecal samples from community cases of diarrhoea and subsequent submission of all positive stools to the CRU for typing to the species level. Thus it was already known prior to the outbreak investigation that the cases were *C. hominis* and that adult cases were represented in excess to that expected. An excess of adult cases has previously been associated
with waterborne outbreaks (Meinhardt et al. 1996). The reason for the excess of female cases is unexplained and might reflect social and or lifestyle differences but this was not further explored. The excess of adult cases suggests that the water supply had not previously been a source of infection for a sufficient period of time to permit an increase in susceptible persons in the population. This is in contrast to experience with other more contaminated, usually lowland, surface water supplies, consumers of which generally show an increased sero-prevalence and lower attack rates in the event of an outbreak (Casemore 2006).

Continuous monitoring was not in place prior to the outbreak because the water company’s risk assessment had not identified Cwellyn WTW as being at significant risk of Cryptosporidium. The anticipated effect of dilution of pollutants in the lake has to be set against the effects of the impact of spate conditions in a mountainous area with heavy rainfall and the effect of short circuiting through streaming and stratification (see accompanying paper). In addition, partial dilution of pollutants can selectively increase the proportion of oocysts in the upper layers of the lake. Such dilution permits the settlement of larger particles of debris while oocysts are too small and insufficiently dense to be subject to Stoke’s law on settlement and tend to remain in suspension (Badenoch 1990). In addition, their negative surface charge (zeta potential) means that they tend to form a mono-suspension rather than aggregating.

It is not possible to be certain about the presence or numbers of oocysts in treated water prior to the beginning of November 2005. Continuous monitoring at Cwellyn WTW from the 2nd November and elsewhere in the water distribution system from 4th November consistently detected low numbers of oocysts. The numbers reported are likely to represent a minimum value although the use of a 24-hour average means that short term fluctuations will not be recognized. Recoveries of oocysts using the standard method are about 40% but under optimal conditions recoveries may be 60–80% (Casemore et al. 2001). Although in some cases recoveries may fall to less than 10% it is likely that consumers were being exposed to only very small numbers of oocysts.

The median incubation period of a C. hominis isolate used in an experimental challenge study is 4 days (range 2 to 10 days) (Chappell et al. 2006) and thus the majority of the 81 primary cases with onset on or after 10th November are likely to have been exposed to low numbers of oocysts. Investigation of water residence time in distribution in this network by stopping the addition of orthophosphate, used as part of normal water treatment, demonstrated rapid decline in phosphate levels in most areas within 6 days and phosphate levels below 0.1 µg/l at the very end of the system by 10 days (J. Cannon, 2007, personal communication). Even the most conservative estimate using a maximum incubation period of 10 days and allowing 10 days for transit of oocysts from the water treatment works to the consumers tap suggest that all of the 30 primary confirmed cases with onsets from 24th November onwards were exposed to very low numbers of oocysts. It is biologically plausible that very small numbers of oocysts might result in disease as the ID50 for C. hominis in health humans is 10 oocysts (Chappell et al. 2006). Thus, half of the population will become infected if exposed to 10 oocysts and some individuals are likely to develop disease after exposure to a single oocyst.

We hypothesise that low numbers of Cryptosporidium oocysts were present in treated water continuously during the outbreak but that these were of sufficient infectivity to cause illness. The shape of the epidemic curve suggests that it is unlikely that a large number of oocysts entered the distribution system prior to the introduction of continuous monitoring and thus later cases cannot simply be explained by transit of a short-term spike through the distribution system. In another outbreak in the UK where C. parvum oocysts persisted in the water distribution despite their removal from the source they did not cause further disease (Howe et al. 2002). It has not usually been possible to relate oocyst numbers to risk level and the numbers found in association with outbreaks has varied widely. Three factors in particular are important: oocyst viability, species of isolate, and immunity of those exposed (Casemore 2006).

Regulatory continuous monitoring only detects and quantifies the number of oocysts present but does not identify the species or determine if these oocysts are viable or capable of causing disease. This explains why both high oocyst counts have been observed in drinking water without any increase in human cases (Hunter 2000) and outbreaks
have occurred in the presence of low numbers of oocysts (Morgan et al. 1995; Willocks et al. 1998; CDSC 1999; Howe et al. 2002; Neira-Munoz et al. 2007). Unfortunately the only way to determine with complete certainty the risk associated with oocysts in treated water is by supplying the water to a large susceptible population. Communicable disease surveillance detects the impact on human health in situations where oocysts counts are very low and the water treatment works is operated in compliance with regulatory requirements and its risk assessment.

The introduction of regulatory continuous monitoring for Cryptosporidium in 1999 was followed by a decrease in outbreaks and sporadic case numbers (Casemore 2003; Sopwith et al. 2005; Lake et al. 2007). There was consequently a tendency in some quarters to regard the treatment standard (1 oocyst per 10 L/1000 L/24 hrs) which applied to works identified as being at significant risk as being effectively a health risk standard although this is an invalid assumption (Lightowlers 2002; Casemore 2004). This had an impact on the initial interpretation of the risk from the low numbers of oocysts detected in the Cwellyn supply. However, the reduction nationally of case numbers, in outbreaks and sporadic (endemic), was partly due to other factors including enhanced formal risk assessments, catchment control, and optimization of treatment, partly aimed at reducing disinfection by-products (Casemore 2005). It has now been recognised that even low numbers of oocysts detected in drinking water can cause substantial disease and the standard has now been revoked under the amended water quality regulations. In addition, the previous regulations also effectively prevented the use of UV or other treatments aimed at killing but not removing oocysts. This has also been amended in the new regulations.

As a result of this outbreak and other events occurring at the same time the DWI required all water companies to review their existing risk assessments and operational risk management arrangements for surface water derived water supplies (DETR 2005). Effective water treatment to remove or kill Cryptosporidium must be considered for all such supplies.

While every care is normally taken by the water industry, the Regulators and public health officials, to ensure the safety of water supplies it is inevitable that from time to time breakdowns may occur in the water treatment and distribution system and a public BWN will need to be issued to protect the public health.

In this outbreak several issues arose concerning the use of the BWN to help limit the outbreak. The decision was taken initially to limit the advice to severely immuno-compromised patients, via clinicians. The decision was based on advice to a sub-group of the IMT that a BWN was not worthwhile given the poor response shown by consumers to this advice (Hunter 2000) and perceived potential risks associated with handling hot water. Our view is that a public BWN in this outbreak was essential especially if applied on a precautionary basis at an early enough stage. Even if only 20–30% of the affected population had responded, that would have been 20–30% fewer exposed. For those who are severely immuno-compromised they should routinely boil their water whatever the source.

We would suggest that the potential “dangers” (e.g. an increased risk of scalds) of a BWN can readily be circumvented, especially since oocysts die well below 100°C and water need only to be raised to the boil. In the domestic setting a standard kettle with a thermal cut-out should meet most needs, with a suitable covered jug in which cooled boiled water is kept in the fridge. The poor response often cited as a reason for not issuing a BWN clearly indicates a failure of communication with and education of the public. Thus, there is a need for more proactive and constructive communication, not abandoning the only immediate control measure available. Suitable public health messages, including the need for increased hand washing, can be promulgated proactively by public health officials via the media, to supplement the advice given by water companies. We would suggest that the public have the right to make an informed choice.

Other consumers will switch to bottled water rather than boiling. It would be prudent in future incidents to make this option more clear as part of the BWN although water companies do provide bulk supplies of bottles to various institutions. Boiled tap water should always be used to prepare bottles of infant formula milk powder.

In the case of commercial users there are several issues:

(i) Catering within canteens and restaurants.
(ii) Commercial vending machines and drinks dispensers, for example post-mix dispensers and hot drinks vending machines that may also deliver cold water. (iii) The impact on the food production industry, especially for food which will not be further heated prior to consumption.

These commercial users need to consider the impact of a possible BWN under their risk assessments and due diligence tests prior to a BWN. The use of point-of-entry or point-of-use filters is one option to avoid the need for heating and then moving large volumes of water with its obvious risk of scalds.

Commercial operators should not assume that it is the sole responsibility of the water companies to ensure that water used in catering and food production will never become contaminated. These potential problems, together with loss of production and consequent impact on food production businesses can be significant. However, the use of point-of-entry (to premises) or point-of-use filters or UV units can readily circumvent the impact of a BWN. This applies especially to foods that will be consumed without further heating. Suitable filters are readily available for fitting to post-mix and other drinks vending machines in canteens and public houses. Filters should be classed as absolute (not nominal) and rated at less than 1.0 micron retention. Care should always be taken to follow manufacturers’ instructions with regard to maintenance and replacement of filter elements.

A further issue was the question of responsibility for issuing the BWN. Although the Group of Experts recommendation was that this should be done in consultation with the IMT/OCT, it is legally the responsibility of the water company. In this case, the water company did not do so because: (i) there appeared to be no identifiable failure of treatment; (ii) oocyst numbers were well below the statutory treatment standard; (iii) the advice from the Group of Experts was that a BWN should only be issued when criteria for its removal have been identified and no such criteria could be agreed in this case. Experience has shown that such criteria cannot always be identified or need to be refined during the course of the investigation (Harrison et al. 2002). In this case there was strong presumptive epidemiological evidence implicating the water in the absence of evidence for water treatment failure; the absence of an event or fault that could be remedied was met by the introduction of UV treatment. We believe that this was the first instance in the UK that this had been done and led to a change in the water quality regulations.

The second report of the Group of Experts (Badenoch 1995) drew attention to the need for regular contact between the various parties and rehearsal of the joint response to incidents and outbreaks. Some of the issues raised underlined the value of this advice and a formal liaison group, the Water & Health Partnership, to coordinate the approach to any future incidents or outbreaks.

A final issue raised was the involvement of the water company in the IMT/OCT. Although this would not be the case in, for example the involvement of a producer or caterer in foodborne infection investigation, the complexity of water collection, treatment and distribution, together with almost universal and continuous exposure of the population in the event of a problem makes their direct involvement essential. This does not preclude the parties to the IMT/OCT holding sub-group meetings to discuss specific issues.

**CONCLUSION**

*Cryptosporidium hominis* outbreaks can occur in the presence of very low numbers of oocysts detected in treated water. The risk to human health may only become apparent when this water is supplied to a large susceptible population resulting in an outbreak. It should be remembered also that the presence of oocysts in the water supply contributes to sporadic disease although the association will usually be difficult to identify except when studies have been set up specifically to look for this (Goh et al. 2004; Goh et al. 2005). All surface water-derived water supplies present a potential risk to human health and appropriate control measures should be in place to minimise these risks. The number of issues raised by the outbreak and its investigation, the lessons learned and the regulatory changes which resulted from this outbreak suggest that there is a need for the Expert Group to be reconvened to consider them.
ACKNOWLEDGEMENTS

We would like to acknowledge the work of all individuals and organisations who contributed to the investigation and management of the outbreak. These include individuals working for Anglesey County Council, Gwynedd County Council, Anglesey Local Health Board, Gwynedd Local Health Board, National Public Health service for Wales, Dwr Cymru/Welsh Water, United Utilities, Drinking Water Inspectorate, Environment Agency Wales, Institute of Geography & Earth Sciences Aberystwyth, NHS Direct, NPHS Microbiology Bangor, UK Cryptosporidium Reference Unit, North Wales Local Health Protection Team.

REFERENCES


Lightowlers, P. 2002 DWI under fire over crypto claims. ENDS Report 301, 8–9.


First received 1 June 2009; accepted in revised form 4 August 2009. Available online 9 November 2009