RAPID RISK ASSESSMENT

Increased *Cryptosporidium* infections in the Netherlands, United Kingdom and Germany in 2012

14 November 2012

Main conclusions and recommendations

An increase in cryptosporidiosis notifications has been observed in the United Kingdom, the Netherlands and Germany since August 2012 that is likely to be real, and not due to surveillance or notification artefacts.

The available information from investigations in the United Kingdom, the Netherlands and Germany indicates that there is not a single, common source, but rather a combination of several causes. These may include climatic drivers, such as the increased rainfall in the summer of 2012 in these countries or a widely distributed commonly consumed product. There is however no evidence for it at this stage and further investigations are ongoing.

The overall threat for the European Union/European Economic Area (EU/EEA) is considered to be low.

EU/EEA Member States should be alert to an increase in cases as observed in the United Kingdom, the Netherlands and Germany, particularly in relation to immunocompromised and other at-risk groups as they may present with a more severe manifestation of cryptosporidiosis.

Source and date of request

ECDC internal decision, 14 November 2012.

Public health issue

Does the increase in incidence of *Cryptosporidium* infections reported by the Netherlands, Germany and United Kingdom in the latter half of 2012 represent a real change in the epidemiological pattern of the disease and could it be related to a potential widely distributed common source of infection in the EU/EEA?

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Disease background information

Cryptosporidium is a microscopic protozoan parasite that causes the diarrheal disease cryptosporidiosis.

There are many species of *Cryptosporidium* that can infect humans and animals. Some species infect mammals including cattle, sheep, rodents, cats and dogs, but also birds, fish and reptiles. *Cryptosporidium* lives in the intestine of infected humans or animals. An infected person or animal sheds a high quantity of *Cryptosporidium* oocysts in faeces.

The disease in humans is predominantly caused by the species *Cryptosporidium* hominis and *Cryptosporidium* parvum, although a number of other species are also pathogenic for humans. Currently, there are 26 recognised species, of which C. hominis (previously known as C. parvum Type 1), found primarily in humans, and C. parvum (previously known as C. parvum Type 2), found in humans and other mammals, are the two major human pathogens and have been reported as cause of morbidity and outbreak of disease.

Ingestion of oocysts, which contain the infective stage of parasites life cycle, can most commonly cause watery diarrhoea in humans and protracted diarrhoea in people with an immune deficiency (e.g. people with AIDS; those with inherited diseases that affect the immune system; and patients who are taking certain immunosuppressive drugs). Symptoms of cryptosporidiosis generally begin two to ten days (average seven days) after becoming infected with the parasite. Symptoms usually last about one to two weeks (with a range of a few days to four or more weeks) in healthy persons. People with weakened immune systems may develop serious, chronic disease that may be life threatening.

The parasite is protected by an outer shell that allows it to survive outside the body and makes it very resistant to severe environmental conditions (heat, cold or chemical disinfectants) for prolonged periods of time. It can remain and survive for months in moist soil or water. The parasite can survive most common water disinfection procedures, including chlorination, therefore water distribution systems and swimming pools are particularly susceptible to contamination with *Cryptosporidium*. The parasite can be effectively removed by well operated filtration, or killed by UV treatment but not by chlorine treatment of water.

Faecal-oral transmission can occur directly through person-to-person and animal-to-person routes or indirectly through environmental vehicles (e.g. contaminated water and food). Ingestion of contaminated drinking water and recreational water is the most common mode of transmission but human to human transmission and zoonotic transmission can also occur. Infective dose is very small and about two to ten oocysts are estimated to be sufficient to cause the disease.

Outbreaks have been reported in healthcare facilities and day-care centres, institutions, at open farms, within households, among bathers and water sports players in lakes and swimming pools, and in municipalities with contaminated public and private water supplies. Most cases are reported in summer months, with *C. hominis* infection predominating in this period.

[1] The views in this document do not necessarily represent the views of the WHO Regional Office for Europe

Food-borne outbreaks of cryptosporidiosis infections have been documented in association with raw or insufficiently pasteurised milk, unpasteurised apple juice, and raw produce, including parsley, green onions, and chicken salad as well as transmission via food handlers. In the USA, there have been several outbreaks linked to apple cider. *Cryptosporidium* oocysts have been detected in bottled water in Brazil and Mexico, but at a low concentration as well as in shellfish, vegetables and fruit.

There is no single test for *Cryptosporidium* infection. The demonstration the of presence of *Cryptosporidium* species oocysts or *Cryptosporidium* antigen in a sample may be sufficient for a positive diagnosis. Diagnosis is established microscopically with acid-fast or fluorescence-based stains. Microscopy alone cannot determine the species of *Cryptosporidium*. Nucleic acid detection tests can provide a greater sensitivity to the species level diagnosis. Species/genotypes and/or subtype identification can be performed on *Cryptosporidium* DNA using molecular techniques, such as the Real time PCR based methods typing and sequencing of PCR products amplified from defined genetic loci (e.g. 18SrRNA, COWP, HSP60, GP60 and microsatellites). This not only confirms diagnosis, but also provides additional discrimination at subspecies level. There is no standardised subtyping scheme for *C. parvum* or *C. hominis*. DNA sequence analysis of the *gp60* gene provides transferrable data for further discrimination but will underestimate diversity as only a single locus is analysed.

Most healthy people will recover without treatment. Treatment aims primarily at reducing symptoms of diarrhoea and preventing dehydration. There is no EU-wide approved medicine for the treatment of cryptosporidiosis in the EU/EEA. Nitazoxanide is approved in the United States for treatment of diarrhoea caused by *Cryptosporidium* in immunocompetent people. The effectiveness of this drug for immunocompetent patients is still under debate. The effectiveness of nitazoxanide in immunosuppressed individuals is unclear.

Event background information

The Netherlands posted an urgent inquiry on the epidemic intelligence information system for food and waterborne diseases (EPIS-FWD) on 25 October to inform European Union/European Economic Area (EU/EEA) Member States (Member States) of an unprecedented increase in reported cryptosporidiosis in faecal samples diagnosed in medical microbiological labs in 2012 compared to previous years. The laboratories report a wide range of increase in the percentage of positive samples (in some of the laboratories there was an increase from 1.5% to 6.5% of positive samples while in others from 1.1% to 12%). A precise estimate of the increase cannot be provided at this stage. A laboratory-based surveillance system for *Cryptosporidium* is lacking. The increase started in August 2012 across the country and continued until week 38. The numbers dropped after week 38 but are still higher than normal in the beginning of November. The most frequently isolated species was *C. hominis* based on the GP60 marker the dominant type 1bA10G2. This type has been the most frequently found type in humans in the Netherlands in recent years. Overall, the age and gender distribution did not differ from previous years. The age distribution of cases has two peaks: 19–65yrs (mostly women), and 0–5yrs (mostly boys in most regions). The National Institute of Public Health and the Environment does not have direct evidence of secondary transmission from parent to child, or child to parent.

England and Wales also reported a large seasonal increase in the reporting of *Cryptosporidium* cases from the end of August 2012, with 2 173 cases reported between weeks 33 to 43 of 2012 across all regions in England and Wales compared to an average of 1 430 cases reported for the same weeks over the previous six years. However there are wide variations observed in the scale of the autumn peak from year to year and it should be noted that the observed reporting levels were at the lower end of the expected range in 2011. *C. hominis* represented 75% of isolates with a high proportion belonging to the 1bA10G2 *gp60* subtype. This is the largest increase in cryptosporidiosis seen since 2003.

Germany has observed a 1.6-fold increase of notified cryptosporidiosis cases in weeks 34 to 39 of 2012 compared to the average of the same time period in the previous five years (386 versus 238 cases). The number of notified cases was highest in week 37 of 2012. Age and gender distribution and the proportion of imported infections did not differ substantially from previous years.

The United Kingdom carried routine case interviews using standard questionnaires in the North East of England in 2012 and did not identify a common source(s) of infection. A higher proportion of infections were observed in those returning from Spain, and to a lesser extent Turkey. Many small outbreaks and case-clusters associated with this time period were also observed, involving recreational water and foreign travel.

The Netherlands carried out a case-control study in September in four regions covering 85 cases and 124 controls. Results from this study had tentative evidence of an elevated risk related to mineral water (odds ratio 2.5 by multivariable analysis); although only 20% cases reported having drank it. There were no questions on specific brands of products. There was no evidence of increased risk from having swum in surface water. Travel abroad is reported by about 36% of cases; the same results for mineral water are seen when these travel-related cases are excluded from the analysis.

Environmental drivers and climatic patterns may explain some of the increase of cases in the UK and the Netherlands as they have experienced heavy rainfalls this summer and autumn. In the Netherlands the temperature was high in the middle of August and beginning of September.

Background data

Cryptosporidiosis is among the 52 diseases and health issues under surveillance in the EU/EEA, and the case-definition for reporting at the EU level is described in Commission Decision 2008/426/EC[2]. It includes clinical, laboratory and epidemiological criteria.

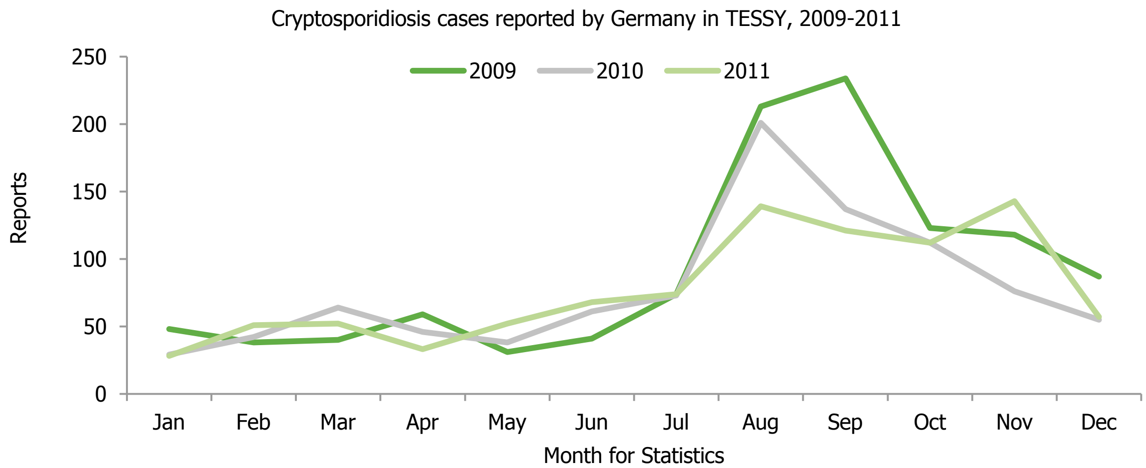
Cryptosporidium data is reported to ECDC into the European Surveillance System database by 21 of the 30 EU/EEA Member States including the United Kingdom and Germany, but not the Netherlands, where the disease is not under surveillance. The other 19 Member States that supply data on cryptosporidiosis cases are Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Estonia, Finland, Hungary, Ireland, Latvia, Lithuania, Luxembourg, Malta, Poland, Romania, Slovakia, Slovenia, Spain, and Sweden. The sensitivity of surveillance systems is believed to vary considerably.

Cryptosporidium data is available in the European Surveillance System from 2005 until 2011.

Only *C. parvum* is notifiable in Germany. However, most laboratories do not perform tests that can discriminate between *C. hominis* and *C. parvum*. Therefore Germany's *Cryptosporidium* data in the European Surveillance System is presumably a mix of *C. hominis* and *C. parvum*. This is also true of the publicly available *Cryptosporidium* data in the Robert Koch Institute's SurvStat database.[3] .

Both species are under established surveillance in the United Kingdom, and so *Cryptosporidium* data in the European Surveillance System represents the total *Cryptosporidium* infections reported in the United Kingdom.

Figure 1. Number of cryptosporidiosis cases reported by month, Germany, 2009–2011 (n=2 970)

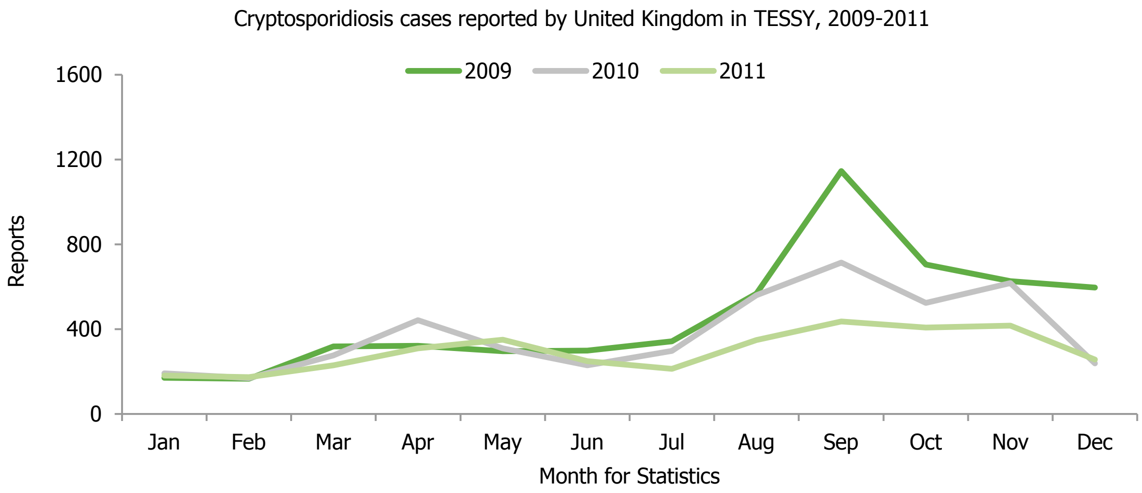


Source: the European Surveillance System, accessed 13 November 2012

[2] Available at: http://eur-lex.europa.eu/Result.do?T1=V4&T2=2008&T3=426&RechType=RECH_naturel&Submit=Search

[3] Available at: http://www3.rki.de/SurvStat/QueryForm.aspx

Figure 2. Number of cryptosporidiosis cases reported by month for, United Kingdom, 2009–2011 (n=13 693)



Source: the European Surveillance System, accessed 13 November 2012

The mean annual number of reports of *Cryptosporidium* cases in the European Surveillance System in 2009 to 2011 was 990 from Germany and 4 564 from the United Kingdom. Monthly data in the European Surveillance System from Germany and the United Kingdom from 2009 to 2011 show increased reports between July and October each year (figure 1 and figure 2).

Information is available for age and gender in Germany and the United Kingdom TESSY data from 2009–2011, with more than 99% of this data complete. The mean age of cases reported by Germany at this time was 23.8 years (range 0 to 97 years) and 19.7 years in the United Kingdom (range 0 to 110 years). Males accounted for 50% of reports in Germany (1 488/1 479), and 46% of reports in the United Kingdom (6 332/7 197).

ECDC threat assessment for the EU

An increase in cryptosporidiosis notifications has been observed by the United Kingdom, the Netherlands and Germany in late summer-autumn 2012. To date, no other countries have reported an unusual increase in reported number of cryptosporidiosis cases. The number of cases is going down although there are still more cases than usual at this time of year in the Netherlands.

According to affected Member States, the increase is unlikely to be due to surveillance or notification artefact. Laboratory and epidemiological investigations are ongoing to explore the cause(s) of this increase.

The available information from investigations in the United Kingdom, the Netherlands and Germany indicates that there is a not a single, common source, but rather suggest a combination of several causes. These may include climatic drivers, such as the increased rainfall in the summer of 2012 in these countries. Further investigation is required to assess this hypothesis.

A widely distributed commonly consumed product may also be a contributing factor for the noted increase. As increased infections were reported over a ten week period, it is unlikely that a product with a short shelf life would be involved, such as a contaminated salad. Infection from contaminated bottled water is a plausible hypothesis for a subset of cases in the Netherlands, but not in the United Kingdom. This is being further explored by the Netherlands.

The overall threat for citizens in the EU is considered to be low. However, Member States should be alert to an increase in cases as observed in the United Kingdom, the Netherlands and Germany, particularly in relation to immunocompromised and other at risk groups.

Conclusions

There has been an unusual increase in cryptosporidiosis notifications in the United Kingdom, the Netherlands and Germany unlikely to be due to surveillance or notification artefact.

The available information from investigations in the United Kingdom, the Netherlands and Germany does not indicate that there is a single common source, and suggests a combination of several causes that are being further explored. These may include climatic drivers, such as the increased rainfall in the summer of 2012 in these countries or a widely distributed commonly consumed product. There is however no evidence for it at this stage and further investigations are ongoing.

The overall threat for the EU is considered to be low.

Member States should be alert to an increase in cases as observed in the United Kingdom, the Netherlands and Germany, particularly in relation to immunocompromised and other vulnerable population groups.

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