衞生防護中心
Centre for Health Protection

Scientific Committee on Enteric Infections and Foodborne Diseases

Epidemiology, Prevention and Control of Cryptosporidiosis in Hong Kong

Purpose

This paper reviews the latest global and local epidemiology of cryptosporidiosis, and examines the current prevention and control measures of the disease in Hong Kong.

Background

2. Cryptosporidiosis is a diarrhoeal disease caused by microscopic parasites called *Cryptosporidium*. The first human case of cryptosporidiosis was reported in 1976, and the disease emerged in the 1980s as an opportunistic infection in patients with Acquired Immunodeficiency Syndrome (AIDS)[1, 2]. It is now widely recognised as a common parasitic cause of acute diarrhoeal disease in healthy individuals, and an important cause of severe diarrhoea in young children and immunocompromised people[3,

The Parasite and Its Life Cycle

3. *Cryptosporidium* is a protozoan parasite. Currently, 26 species of *Cryptosporidium* have been identified[5]. Among the species that infect human, *Cryptosporidium hominis* (*C. hominis*) and *C. parvum* are responsible for over 90% of human infections[6]. Human infections of other species such as *C. canis*, *C. felis*, *C. meleagridis*, *C. muris and C. viatorum* have also been reported but less frequently[7, 8]. *C. hominis* is mainly spread through human-to-human transmission, while *C. parvum* spreads from human to human or from animal to human[9]. Many animals, particularly cattle, can be potential reservoirs of zoonotic infection of *Cryptosporidium*[5]. The geographic distribution of *Cryptosporidium* species in human varies around the world. Literatures suggested that *C. hominis* was the dominate species in most parts of the world, particularly in developing countries, whereas *C. parvum* was prominent in the Middle-East. In European countries, both *C. parvum* and *C. hominis* were commonly found in humans[10, 11].

4. *Cryptosporidium* has a complex life cycle that includes both asexual (mitosis) and sexual (meiosis) stages in a single host[10]. The parasite does not reproduce outside of a host. It is infectious through faeces excreted by the infected host. The parasite is excreted as sporulated (mature, infective) thick-walled oocysts with small sizes of 4 to 6μm in diameter[12]. Each oocyst contains four sporozoites. After the oocysts are ingested by a host, excystation occurs when the oocysts reach the gastrointestinal tract and infective sporozoites will be released. Sporozoites attach to and invade the intestinal epithelial cells. The parasites then undergo asexual multiplication and followed by sexual multiplication within the brush border of the epithelial cells where microgamonts (male) or macrogamonts (female) are produced. Upon fertilisation of the microgamont and macrogamont, two different types of oocysts are developed from the zygote, namely thick-walled and thin-walled oocysts. The thick-walled oocysts are excreted into the environment from the host while the thin-walled

oocysts excyst within the same host and start a new infection cycle (autoinfection) (Diagram 1)[7, 10].

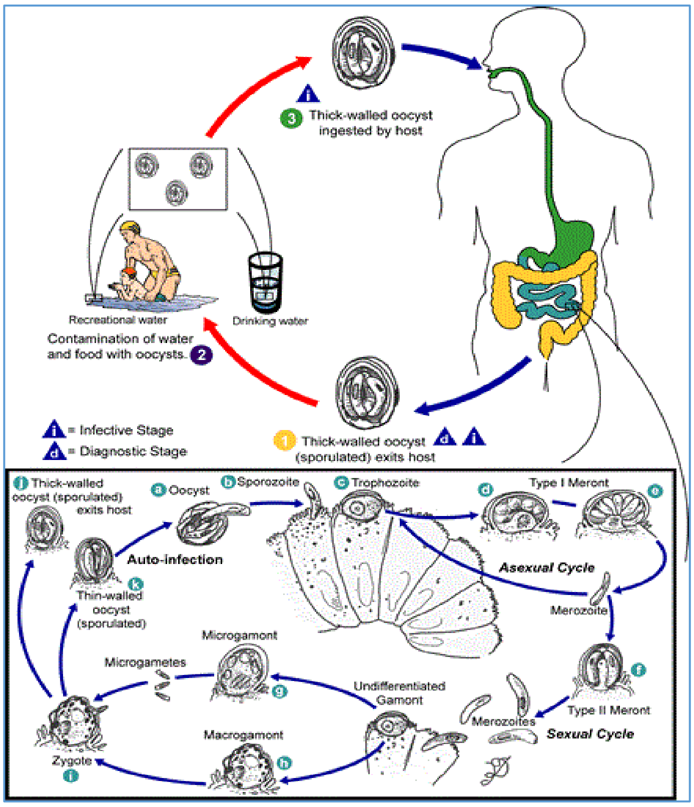

Diagram 1. Life cycle of *Cryptosporidium* species (source: United States Centers for Disease Control and Prevention).

Disease Transmission

5. Cryptosporidiosis is transmitted through faecal-oral route either directly or indirectly. Once *Cryptosporidium* oocysts are excreted in faeces from an infected host to the environment, they can be transmitted to a new host through direct contact, or indirectly through ingesting faecally contaminated water, swallowing contaminated recreational water while swimming, ingesting crops irrigated with contaminated water, etc[11].

6. In general, infected persons can shed 10^7-10^8 oocysts in a single bowel movement and can continue to excrete infectious oocysts for up to 60 days after gastrointestinal symptoms resolved[12]. The transmission is facilitated by the low infective dose, with as few as ten oocysts being able to cause infection in a healthy individual[13-15]. Besides, the oocysts are protected by thick walls that enable them to survive and remain infectious in moist environment for at least 6 months[11]. Of note, *Cryptosporidium* oocysts are extremely resistant to most of the disinfection processes in water treatment system such as chlorination, but they can be removed by treatment processes like coagulation, sedimentation and filtration[9, 10]. It is also found that ultra-violet irradiation and ozone are more effective disinfectants than chlorine for inactivation of *Cryptosporidium* oocysts[16].

Clinical Presentation

7. Cryptosporidiosis is generally a mild and self-limiting disease but can be severe in children and immunocompromised persons. The incubation period ranges from two to 10 days with an average of seven days[17]. Immunocompetent people infected with *Cryptosporidium* can be asymptomatic or present with mild and self-limiting symptoms that last for one to two weeks[12]. Symptoms include watery and non-bloody diarrhoea that can present as five to 10 episodes of watery diarrhea per day with mucus flecks. Other symptoms include abdominal pain, dehydration, nausea, vomiting, fever and weight loss[9, 12]. Patients might experience a recurrence of symptoms after apparent resolution[6].

8. In immunocompromised individuals such as patients with AIDS, cancer patients or transplant recipients who are taking immunosuppressive drugs, the symptoms can be more severe and prolonged and may lead to serious or life-threatening illnesses[12, 18]. The severity of the disease depends on the site of infection and the CD4+ T-cell count, with infection usually being more severe

when the count is below 200 cells/mm^3 [19]. While intestinal tract is the most common site of infection, extraintestinal cryptosporidiosis has been reported in patients with AIDS[20]. Other organs such as lungs, biliary tract and pancreas may also be affected, but these sites are likely to be extensions of a primary intestinal infection[19]. Mortality associated with cryptosporidiosis is uncommon in immunocompetent population and outbreak data indicated that the case fatality rate was lower than 1 in 100 000[21, 22].

Laboratory Diagnosis

9. Cryptosporidiosis can be confirmed by detecting *Cryptosporidium* oocysts in stool specimen through three main diagnostic techniques[9, 11] :

(a) microscopic examination, such as acid-fast staining and direct fluorescent antibody (DFA) testing;

(b) Antigen detection methods, such as enzyme-linked immunosorbent assay (ELISA);

(c) Molecular tests, such as polymerase chain reaction (PCR).

10. Different species of *Cryptosporidium* are morphologically indistinguishable but can be identified using molecular methods[23].

Patient Management

11. There is no specific treatment for cryptosporidiosis and the principle of management is to prevent dehydration by drinking adequate amount of fluids. Most immunocompetent patients with cryptosporidiosis recover without treatment. Nitazoxanide has been approved by the United State Food and Drug Administration in 2005 for the treatment of diarrhoea caused by C*ryptosporidium*, but its effectiveness in immunosuppressed patients is unclear[4,

[24, 25]. For HIV/AIDS patients, symptoms may be reduced or eliminated by improving the immune status with anti-retroviral therapy. However, cryptosporidiosis is often incurable in AIDS patients and symptoms may return if the immune status worsens[26]. Thus far, no effective vaccine is available to prevent cryptosporidiosis [11].

Epidemiology

Global Situation

12. Cryptosporidiosis is endemic worldwide but disproportionately affects children in developing countries and immunocompromised individuals[11]. Various studies have found high prevalence rates of cryptosporidiosis in young children who sought medical care due to diarrhoea in developing countries, ranging from 5.9% to 25%[27-33]. A recent systematic review and meta-analysis of 106 studies on the prevalence of *Cryptosporidium* in HIV-infected people found a pooled prevalence of 14% (95% confidence interval: 13.0-15.0%)[34]. In developed countries, *Cryptosporidium* is a common cause of waterborne outbreaks.

United States

13. In the United States (US), the largest outbreak occurred in Milwaukee, Wisconsin in 1993. The outbreak was caused by contamination of Lake Michigan with *Cryptosporidium* oocysts that could not be adequately filtered at one of the water treatment plants, resulting in the parasites entering the drinking water supplies. In this outbreak, more than 400 000 people were affected with 54 fatal cases recorded, of which, 85% had AIDS listed as the underlying cause of death[22, 35]. Since 1995, cryptosporidiosis has become a national notifiable disease in the US[36]. Between 2009 and 2017, 444 cryptosporidiosis outbreaks were reported from 40 states and Puerto Rico, with

an average of 13% increase in the annual number of outbreaks per year over this period (Figure 1)[37]. A total of 7 465 persons were affected, with 287 hospitalisations and one death. Over 40% (n=183) of the outbreaks were associated with the use of recreational water, and the majority of the patients were infected through the use of treated recreational water (n=156, 85.2%) including swimming pool (n=100, 64.1%). This explained the reason for more outbreaks reported in the summer months (July and August). Besides, around one-fifth of the outbreaks were transmitted from person-to-person in institutional settings (n=88, 19.8%) or through direct animal contact (n=86, 19.4%). Foodborne and environmental transmissions were also recorded, accounting for 5% and 0.5% of the outbreaks respectively. The incriminated food items included unpasteurised milk, unpasteurised apple cider and fresh produce [37].

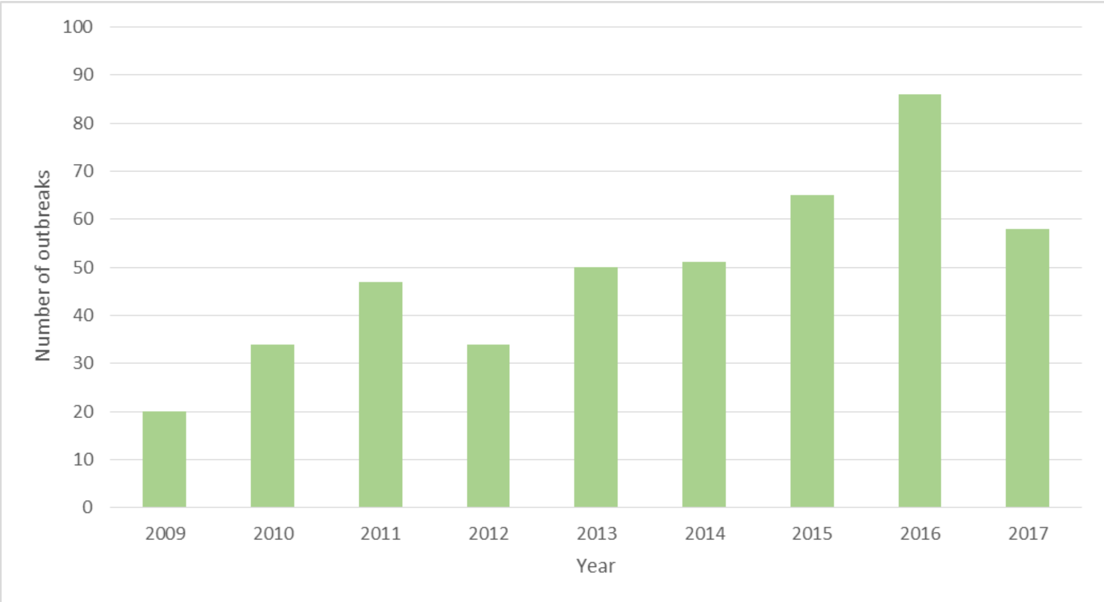

Figure 1. Annual number of cryptosporidiosis outbreaks (n= 444) in the US, 2009-2017[37].

Europe

14. An increasing trend of cryptosporidiosis notification rate was observed in European countries from 2012 to 2016[38]. In 2017, the notification

rate decreased for the first time since 2012. This was largely due to the decrease in number of cases in the United Kingdom (UK), as the UK alone accounted for 44% of all confirmed cases among the 21 reporting countries in Europe[39]. In spite of the overall decrease, some reporting Nordic countries had remarkable increase in the reported number of cases, with more than 3-fold increase in Finland from 2016 to 2017.

United Kingdom

15. In England and Wales, *Cryptosporidium* is an infective agent notifiable to Public Health England (PHE). Diagnostic laboratories have a statutory duty to notify PHE of positive detections of *Cryptosporidium* under the Health Protection (Notification) Regulations 2010[40]. From 2008 to 2017, the annual number of cases identified in England and Wales ranged from 2 990 to 4 292 (median= 4 227) with an annual incidence rate ranging from 5.3 to 10.2 per 100 000 population (median = 7.5 per 100 000 population) (Figure 2)[41]. A study identified 178 *Cryptosporidium* outbreaks in England and Wales between 2009 and 2017, involving 4 031 laboratory confirmed cases[42]. Of the 178 outbreaks, 82 (46%) were related to recreational water while 74 (42%) were related to animal contact. Other sources of infection included environmental contact (2%), person-to-person spread (2%), contaminated food (1%), drinking water supplies (1%) and 5% were unknown. Among the 131 outbreaks (74%) with *Cryptosporidium* species identified, *C. hominis* were predominantly found in recreational water outbreaks (88%), while outbreaks caused by animal contact were exclusively *C. parvum*. A large foodborne outbreak of *C. parvum* associated with consumption of fresh pre-cut salad leaves was reported in 2012, with 74 laboratory confirmed cases[43].

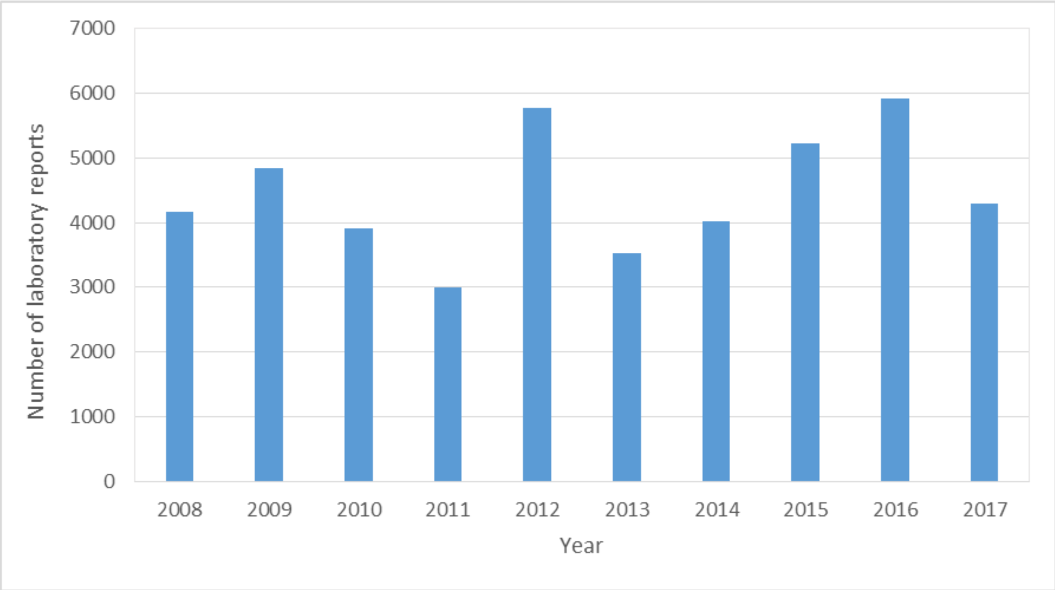

Figure 2. Annual laboratory reports of *Cryptosporidium* in England and Wales, 2008 to 2017.

16. In Scotland, 509 and 536 laboratory reports of *Cryptosporidium* were received by Health Protection Scotland in 2017 and 2018 respectively[44]. Of the isolates speciated in 2018 (n=176), 120 (68.2%) were *C. parvum*, 54 (30.7%) were *C. hominis* and two (1.1%) were *C. cuniculus*.

Australia

17. In Australia, cryptosporidiosis is a national notifiable disease. It is the third most commonly notified gastrointestinal infection in Australia, following campylobacteriosis and salmonellosis. Based on the annual report of the National Notifiable Disease Surveillance System published by the Department of Health of Australia in 2019, there were 4 064 cases of cryptosporidiosis notified in 2015, with a notification rate of 17.1 per 100 000 population[45]. There has been an increase in notification rate during 2010 – 2015 except in 2014 (Table 1). About one third (33%) of the notified cases in 2015 affected children aged under five years. There was an outbreak involving 30 people reported in Victoria in 2015[46]. Most cases had history of recreational water exposure, in particular a waterpark in Victoria.

Year	Number of notified cases	Notification rate per 100 000 population
2010	1 482	6.7
2011	1 812	8.1
2012	3 143	13.8
2013	3 851	16.7
2014	2 408	10.3
2015	4 064	17.1

Table 1. Notified cases and notification rates for cryptosporidiosis in Australia, 2010-2015[45].

Mainland China

18. In Mainland China, information on the epidemiology is limited as cryptosporidiosis is not a notifiable disease and *Cryptosporidium* is usually not a routine testing item for cases of diarrhoea[47]. A literature review published in 2017 estimated the prevalence of cryptosporidiosis among the general population ranged from 1.3% to 13.5%[48]. A study conducted at the paediatric clinic and intestinal clinic of a hospital in Shanghai has found that around 13.5% of the faecal specimens from diarrhoeal patients were positive for *Cryptosporidium*[49]. A study revealed that *C. hominis* was the dominant *Cryptosporidium* species found in human in Mainland China[50]. Another study proposed that drinking water was one of the major sources of *Cryptosporidium* infection in Mainland China and the risk of human exposure to *Cryptosporidium* could be reduced by improving the drinking water treatment systems[51].

Local Situation

19. In Hong Kong, cryptosporidiosis is not a notifiable disease. It is one of the communicable diseases of topical public health concern and medical practitioners are encouraged to report suspected or confirmed cases to the Centre for Health Protection (CHP) of the Department of Health (DH) for investigation.

20. From 2010 to 2019 (as of 31 October), a total of 44 cryptosporidiosis cases were reported to the CHP. The overall trend of the disease was at low level between 2010 and 2014, with zero to one case reported annually (incidence rate: 0.01 per 100 000 population). Since then, there was an upsurge in reported cases, from three in 2015, six in 2016, seven in 2017 to 15 cases in 2018. The incidence rates increased from 0.04 per 100 000 population in 2015 to 0.2 in 2018. In 2019, as of 31 October 2019, nine cases of cryptosporidiosis have been recorded (Figure 3).

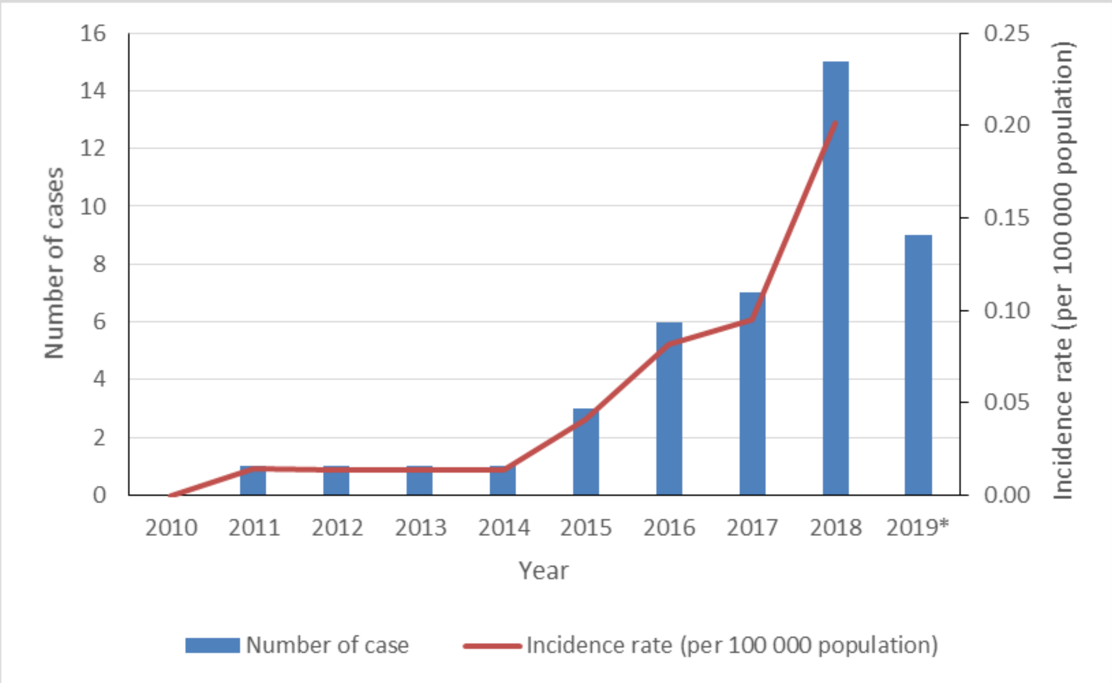

Figure 3. Annual number and incidence rate of cryptosporidiosis cases reported from 2010 to 2019 in Hong Kong. (*as of 31 October 2019)

21. Among the 44 cases, there were 24 males (54.5%) and 20 females (45.5%), with ages ranged from nine to 57 years (median=34 years). Over 70% (n=31) of the affected persons were aged between 25 to 44 years (Figure 4). The patients were mainly Chinese (n=39, 88.6%), while three were Europeans (6.8%) and one was African (2.3%). The ethnicity of the remaining case was unknown as the patient could not be contacted.

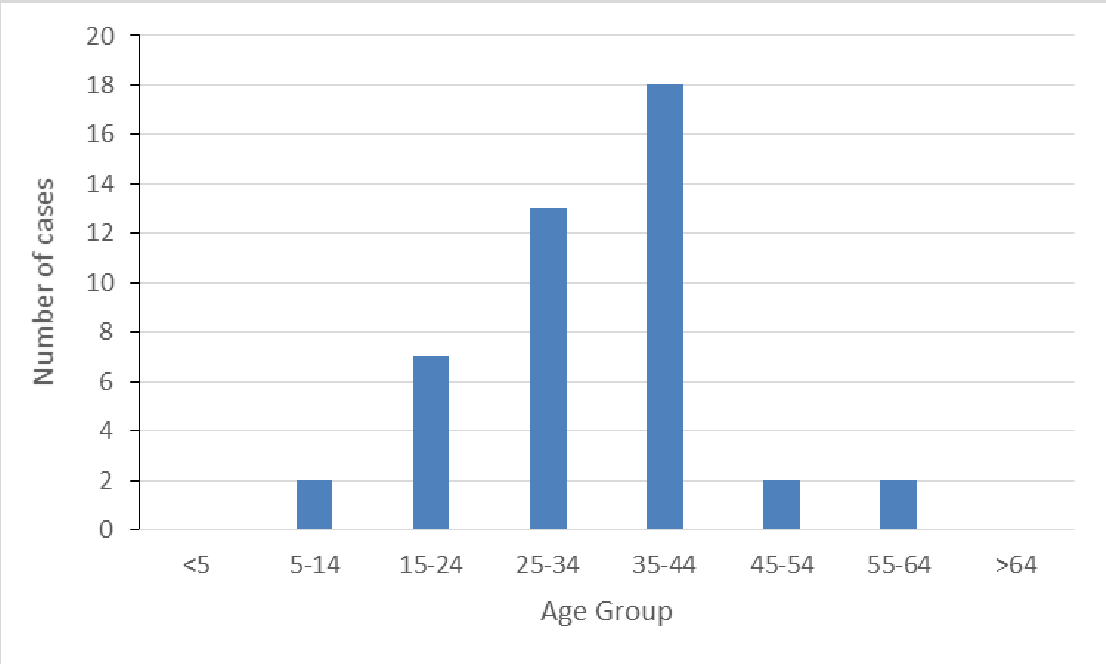

Figure 4. Age distribution of cryptosporidiosis cases in Hong Kong, 2010 -2019 (as of 31 October 2019)

22. Most of the cases acquired the disease locally (n=30, 68.2%), while five (11.4%) were imported cases with travel history to China (n=1), Kenya (n=1), Malaysia (n=1) and multiple countries (n=2). The importation status of eight cases (18.2%) could not be ascertained as they had stayed both locally and overseas during the incubation period. Importation status of the remaining case remained unknown as the patient could not be contacted.

23. Regarding the past medical history of the cases, over half of them enjoyed good past health (n=23, 52.3%). Of note, about 30% of the cases were HIV carriers (n=13), with seven of them known to be men who have sex with men (MSM). One patient had organ transplant performed and was receiving immunosuppressant before the onset of symptoms. One patient had acute leukaemia. Five patients had other underlying medical illness (11.4%).

24. Most cases presented with mild symptoms such as diarrhoea (n=44, 100%), abdominal pain (n=37, 84.1%), fever (n=22, 50%), nausea (n=16, 36.4%) and vomiting (n=15, 34.1%). Forty cases (90.9%) required hospitalisation. Nonetheless, the majority of cases recovered uneventfully except two patients who died of other underlying diseases. Investigations did not identify any epidemiological linkages among the cases. Three cases were healthcare workers while no cases involved food handler.

25. During 2010-2015, all cryptosporidiosis cases were reported from public hospitals or through CHP's Public Health Laboratory Services Branch (PHLSB). Since 2016, more cases were reported from private hospitals (Figure 5) with the majority being initially diagnosed by PCR. Regarding laboratory tests, more than half of the cases (n=25, 56.8%) were first screened and tested positive for *Cryptosporidium* by PCR and subsequently confirmed by microscopy of the stool specimen, with all except one reported from private hospitals. The remaining cases (n=19, 43.2%) were confirmed by direct microscopy of stool specimen, and were reported from public hospitals.

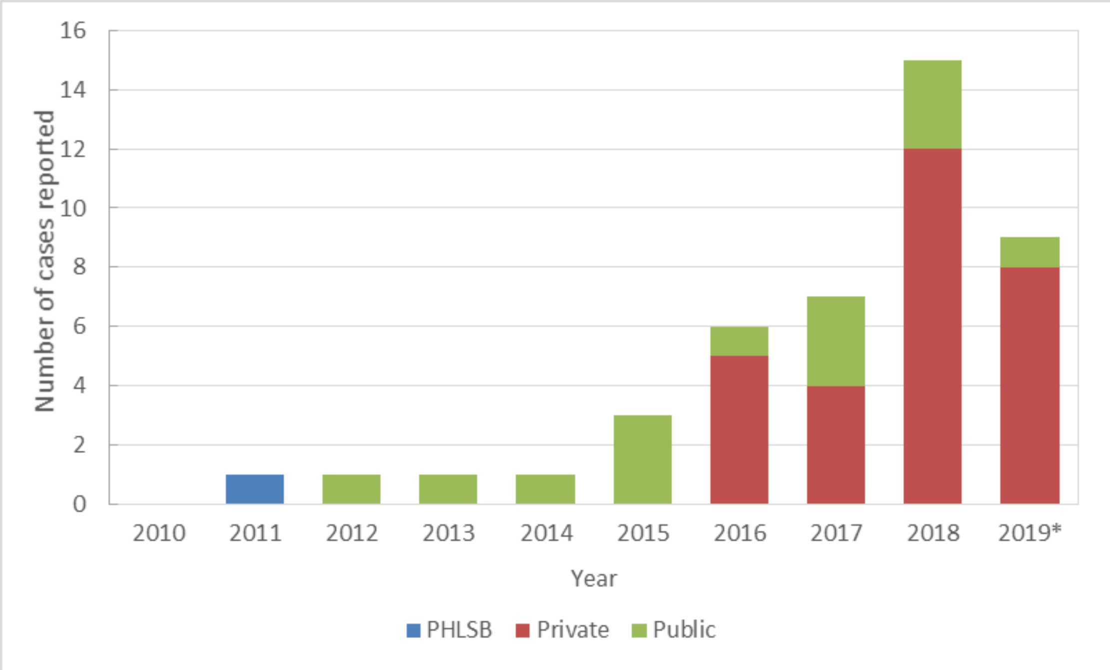

Figure 5. Reporting sources of cryptosporidiosis from 2010 to 2019 (*as of 31 October)

26. There was an upsurge of cases in late 2018, with a total of 12 cases reported in November and December (Figure 6). CHP conducted extensive investigations attempting to identify the reason accounting for the upsurge. All cases had no known exposure history to recreational water or unboiled water. So far, no epidemiological linkage and common exposure among the cases could be identified. Excluding this upsurge, in general there were more cases reported in the latter half of the year from 2010 to 2017.

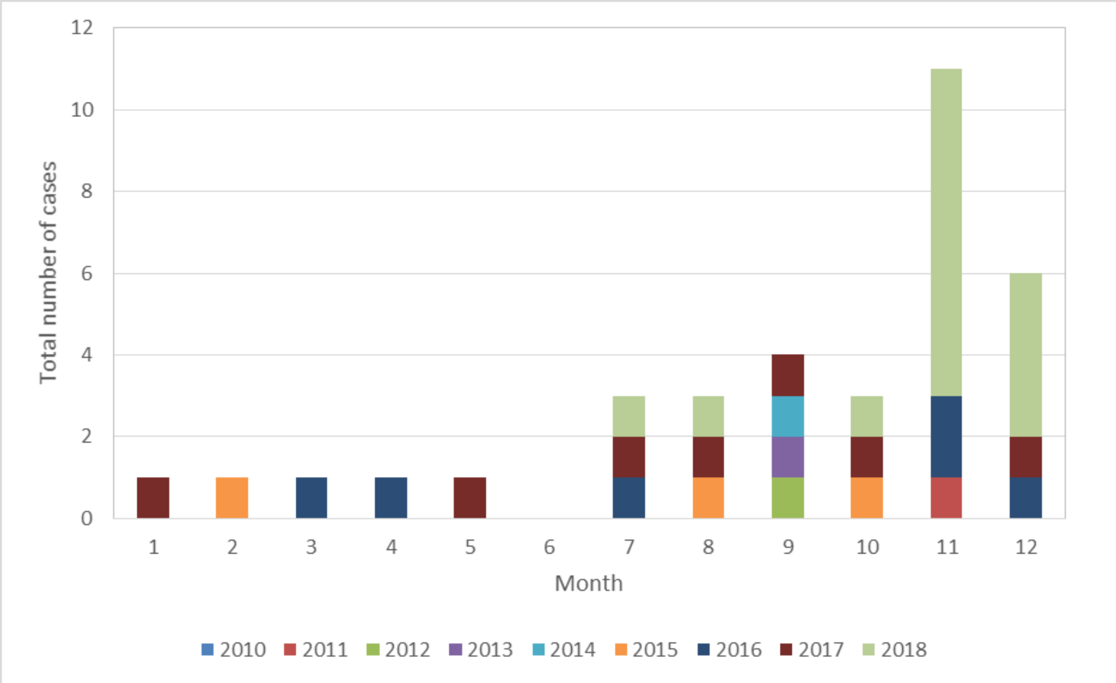

Figure 6. Seasonal pattern of cryptosporidiosis in Hong Kong, 2010 to 2018.

Prevention and Control Measures

<u>Drinking Water</u>

27. In Hong Kong, the Water Supplies Department (WSD) is responsible for providing safe and wholesome potable water supply. Through a series of water treatment processes, raw water is treated to safe drinking water (Diagram 2).

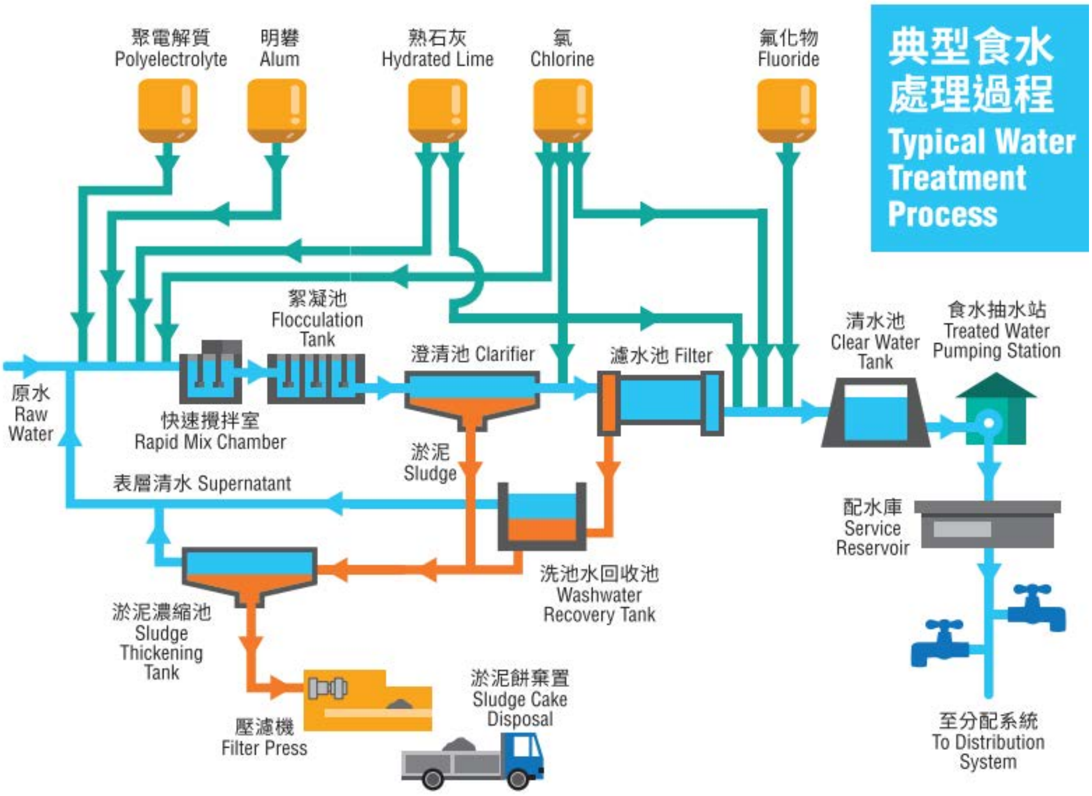

Diagram 2. The water treatment process in Hong Kong. (Source: Water Supplies Department)[52]

28. In Hong Kong, about 99.9% of domestic households are supplied with treated water from WSD. The quality of drinking water provided has to comply fully with the Hong Kong Drinking Water Standard (HKDWS). There is **neither** standard in the HKDWS nor guideline in the "Guidelines for Drinking-water Quality, World Health Organization" published in 2017 for *Cryptosporidium* oocyst in drinking water.

29. WSD has implemented a comprehensive routine monitoring programme for *Cryptosporidium* and *Giardia* to monitor the raw water sources and treated water supplies at selected locations. Monitoring locations and frequencies are based on the strategic importance of the location, the supply quantity, quality and risk assessment of the raw water source, output of the water treatment works and effectiveness of the treatment barrier. Water samples are

also sent to the WSD's subcontracting laboratory for inter-comparison. According to the monitoring results from WSD during the period of April 2018 to March 2019, no *Cryptosporidium* oocyst was detected in all drinking water samples[53].

30. Other water quality monitoring parameters such as continuously high turbidity of treated water at water treatment works can give early warning of particle breakthrough and alert operators for remedial actions to optimise the treatment processes. In addition, the use of indicator organisms, typically *Escherichia coli* (*E. coli*) or faecal coliforms, for faecal contamination is an accepted practice for monitoring and assessing the microbial safety of water supplies.

31. WSD provides the monitoring data and compliance status of treated water supply to the DH on a quarterly basis and will notify DH immediately for any non-compliant result. Task group meetings on health-related issues concerning drinking water quality between DH and WSD are held on a half-yearly or as-needed basis to review and discuss the drinking water quality, emerging concerns and related public health issues.

Recreational Water

32. Contaminated recreational water is a significant source of *Cryptosporidium* infection in developed countries[54]. Recreational water includes swimming pools, wading pools and spa pools.

33. In Hong Kong, the 44 public swimming pools are under the management of the Leisure and Cultural Services Department (LCSD) in accordance with the Public Swimming Pools Regulation (Cap.132BR). The Food and Environmental Hygiene Department (FEHD) licenses and regulates

private swimming pools in accordance with the Swimming Pools Regulation (Cap. 132CA) but this Regulation do not apply to any swimming pool which serves not more than 20 residential units and to which the public have no access.

34. The public swimming pools of LCSD have well-developed filtration and sterilisation systems in place, which continuously filter and sterilise the pool water throughout the opening hours. Dedicated LCSD staff would take pool water samples on an hourly basis to check the level of residual chlorine and pH value, while accredited independent laboratories commissioned by LCSD would collect and test pool water samples every week to ensure the pool water is up to hygiene standards[55]. The acceptable standard includes: (i) total bacterial count not exceeding 200 bacteria per mL of pool water sample; (ii) *E. coli* not detected per 100mL of pool water sample; and (iii) *Vibrio cholerae* not detected per 100mL of pool water sample[56].

35. For private pools issued with swimming pool license, such as those operated by clubs or institutions, FEHD conducts inspections and collects swimming pool water samples on a monthly basis for bacteriological examination during the months of April to October or such other period as the pools are open for use. Pool water samples are collected once a year for chemical analysis to ascertain compliance with the statutory water quality standards. Regarding the water quality standard, the licensees shall maintain the water quality of the swimming pools to meet the standard according to section 10 of the Regulation. The microbiological standard required are: (i) *E. coli* is absent in the pool water samples of 100mL each; and (ii) the total bacterial count does not exceed 200 bacteria per mL of pool water sample[57].

36. The Infection Control Branch of CHP has published "Guidelines on Infection Control of Commercial Spa Pools" (the Guidelines) in 2008 with revisions in 2016 and 2017[58]. The Guidelines recommends methods of

management of spa pools to control the risk of infection, including cleaning and disinfection procedures during faecal contamination incidents potentially with chlorine-resistant pathogens (e.g. *Cryptosporidium*). FEHD licenses and regulates commercial bathhouse in accordance with the Commercial Bathhouses Regulation (Cap. 132I). Licensed commercial bathhouses are inspected at least once in every five months. Spa pool water samples are collected for bacteriological examination during the inspection and the microbiological standard adopts those specified in the Guidelines.

Disease Surveillance and Public Health Response

37. The CHP has an established mechanism for the surveillance of cryptosporidiosis. Upon receipt of notification of a cases of cryptosporidiosis, the CHP would carry out epidemiological investigation and public health control measures immediately.

38. Cases are defined as persons with compatible clinical features with either:

(a) Detection of oocyst by microscopic examination in stool, intestinal fluid or small-bowel biopsy specimens; or
(b) Detection of oocyst or sporozoite antigens by immunodiagnostic methods, e.g. ELISA, or by PCR techniques when routinely available; or
(c) Demonstration of reproductive stages in tissue preparations.

39. A protocol for cryptosporidiosis is in place for epidemiological investigation of reported cases. The patient and his/her attending physician would be interviewed for relevant clinical and epidemiological information. Detailed food, travel, animal and other risk factors exposure history including recreational water use would be elicited. Accidental faecal release during use of recreational water environments, high risk sexual practice and MSM and/or HIV status would be explored. Close contacts such as household contacts and travel collaterals would also be traced.

40. Health education on disease transmission, personal, environmental and food hygiene, with emphasis on hand washing after defaecation and before preparing food, would be provided to the patients and their close contacts. Patients would be advised not to swim for at least two weeks after diarrhoea has stopped, and avoid swallowing water while swimming. To prevent further spread of the disease, necessary measures would also be taken to correct the situation when a source is identified, and the CHP will communicate and collaborate with various departments depending on the source of infection as appropriate.

41. Moreover, DH and WSD has formulated a "Contingency Plan for *Cryptosporidium* & *Giardia* in the Treated Water Supply", which lays down the procedures to be implemented when *Cryptosporidium* oocysts are detected in the treated water supply in Hong Kong.

Conclusion

42. The number of confirmed case of cryptosporidiosis in Hong Kong has been increasing in the past years, and similar trend has been observed in many other countries. The increasing trend could be attributed to increased case detection due to the availability and wider use of more sensitive diagnostic tests (e.g. PCR). With climate changes leading to more extreme weather conditions, the number of outbreaks is expected to increase[59, 60]. It is important to continue monitoring the situation and implement timely control measures.

43. As there are limited options available for prophylaxis and therapeutic treatment of cryptosporidiosis, the best way to prevent and control the disease would be by maintaining the quality of both drinking water and recreational water. The current water treatment and monitoring systems managed by the WSD is important in safeguarding the quality of drinking water provided to the Hong Kong population; the LCSD and FEHD also strive for clean and safe recreational water to be enjoyed by the public in Hong Kong.

44. Lastly, public awareness for the disease and its transmission should be raised, especially among high risk groups such as MSM and immunocompromised individuals. The CHP will continue to promote personal, food and environmental hygiene through various media and channels, and keep abreast of the latest evidence and international practices on effective strategies in the surveillance, prevention and control measures of cryptosporidiosis.

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