衞生防護中心
Centre for Health Protection

Scientific Committee on Enteric Infections and Foodborne Diseases

Prevention and control of amoebic dysentery in Hong Kong

Purpose

This paper reviews the latest global and local epidemiology of amoebic dysentery, examines the current prevention and control measures of the disease in Hong Kong and makes recommendations on further enhancement of the prevention and control strategy.

The pathogen and the disease

2. Amoebic dysentery is an intestinal infection caused by *Entamoeba histolytica* (*E. histolytica)*, a protozoan parasite that exists in either cyst form or trophozoite stage. *E. histolytica* cyst is spherical, usually 10 to 16μm in diameter and is surrounded by a refractile chitin-containing wall. It contains four nuclei when mature, one nucleus when immature with glycogen in a vacuole and often with chromatoid bodies. The trophozoites, sized ranged from 20 to 40μm in diameter, are highly motile (5, 6). The cysts can remain alive outside the host for weeks or months as they were protected by the wall, and the survival time could be longer especially in moist conditions such as water, soil and on foods (1).

3. Among the species in the genus Entamoeba, *E. histolytica*, *E. dispar*, and *E. moshkovskii* can be found in the human intestine. *E. histolytica* is pathogenic and capable of causing invasive infections. *E. dispar* is a commensal organism, while the pathogenicity of *E. moshkovskii* awaits further confirmation (2-4) (Table 1).

Table 1. Pathogenicity of amoebae (3)

	Pathogenic	Non-pathogenic
Amoebae	*Entamoeba histolytica*	*Entamoeba dispar*
		*Entamoeba moshkovskii**
		Entamoeba coli
		Entamoeba hartmanni
		Entamoeba chattoni
		Entamoeba nana
		Iodamoeba butschlii

**Pathogenicity uncertain*

Life cycle and pathogenesis

4. Cysts and trophozoites of *E. histolytica* are passed in faeces. People are infected through ingestion of mature cysts in food or water contaminated with faecal matter, or in contact with contaminated hands. The mature cysts can survive in gastric acidity and then pass to the small intestine or colon where excystation occurs that releases cysts and trophozoites. In fact, cysts are not invasive but the trophozoites are. The trophozoites migrate to the large intestine and invade the intestinal mucosa by depletion of the protective mucus blanket and proteolytic disruption of tissue that cause lysis and necrosis of mucosal cells that induce characteristic flask-shaped lesions (7). In the large intestine, the trophozoites multiply by binary fission and cysts are produced. Both are passed to the faeces subsequently. In severe cases, trophozoites pass from the colon through the bloodstream to extraintestinal sites such as the liver, brain, and lungs that cause pathologic manifestations (8, 9).

Disease transmission and clinical presentation

5. Amoebic dysentery is transmitted through faecal-oral route, either directly from person-to-person contact (e.g. by diaper-changing or anal sex contact) or indirectly by eating or drinking food or water contaminated with faecal matter (10, 11). Human are the main reservoir. People infected are usually asymptomatic and become carriers who can excrete 15 million cysts in the stool per day (12, 13). Incubation period varies from a few days to several months or years but is commonly 2- 4 weeks (13). Several groups of people are at high risk of infection including immigrants from and travellers to developing countries with poor sanitary conditions, peoples living in institutions with poor sanitary conditions and men who have sex with men.

6. The clinical spectrum is wide which can range from asymptomatic to transient intestinal inflammation to fulminant colitis and extraintestinal manifestation. Up to 90% of *E. histolytica* infections are asymptomatic and self-limiting (2). For symptomatic cases, the symptoms are usually mild with diarrhoea, frequent but small volume dysentery, and stomach cramping. Chronic infection can present with gastrointestinal symptoms with fatigue, weight loss and occasional fever. Although extraintestinal infection is not common, it is possible when the trophozoites spread to other organs such as the liver and result in amoebic liver abscess (14). There may also be other complications such as inflammation of the intestine or rarely perforation. Individuals with damaged or impaired immunity such as pregnancy, immunocompromised, or receiving corticosteroids may suffer more severe forms of the disease (8).

Laboratory diagnosis

7. For symptomatic cases, diagnosis mainly relies on microscopic examination of stool or colonic biopsy of patients. Microscopy is time consuming, labor intensive and requires high level of skill and expertise. Besides, diagnosis can be missed as excretion of trophozoites and cysts in stool can be intermittent. A study reported that the sensitivity of microscopy was less than 60%. In addition, microscopy cannot distinguish between *E. histolytica* and *E. dispar* and *E. moshkovskii*. In countries where the frequency of non-pathogenic *Entamoeba* spp. is high, dysentery due to other pathogens such as shigellosis or campylobacter may be misdiagnosed as amoebic colitis if microscopy is the sole diagnostic criterion.

8. Alternatively, there are commercially available antigen detection tests that identify *E. histolytica* antigens in stool and importantly, can distinguish *E. histolytica* from other non-pathogenic *Entamoeba* species. Additionally, serologic tests can help diagnose extraintestinal infection of *E. histolytica* (2, 10). These methods are also much less user dependent. Polymerase chain reaction (PCR) is also available and being increasingly used.

Patient management

9. Antibiotic treatment is needed for both symptomatic and asymptomatic infections of *E. histolytica*. For symptomatic cases, the use of nitroimidazoles is the mainstay of treatment while broad-spectrum antibiotics should be added to cover the colonic flora in fulminant colitis with or without perforation. Most mild-to-moderate cases respond well to nitroimidazole (15). In some situation, surgical intervention is needed for severe cases such as acute abdomen, gastrointestinal bleeding, or toxic megacolon. Since asymptomatic carriers can pass *E. histolytic* cysts in stool that can infect others and 4%–10% of asymptomatic cases can develop disease within a year if left untreated (10), treatment by luminal agent such as diloxanide furoate or paromomycin is recommended. For symptomatic intestinal infection and extraintestinal disease, treatment with nitroimidazoles should be followed by luminal agent in order to eliminate any surviving organisms in the colon and hence, preventing relapse and spreading of the disease. (10, 16-18)

Global epidemiology

10. Amoebic dysentery is found worldwide but it is endemic in most temperate and tropical climates zones, especially in some developing countries with poor sanitation facilities. According to the World Health Organization (WHO), it was estimated that 10% of the world's population were infected by *E. dispar* or *E. histolytica* that resulted in approximately 50 million cases, 100,000 deaths annually, and was the third leading cause of death due to parasitic disease.

Situations in the US and UK

11. *E. histolytica* infection is not endemic in the United States (US) and United Kingdoms (UK). The number of cases had declined in the US since 1985, from 4433 cases to 2983 cases in 1994, with no large scale outbreaks reported in that period. This disease has been removed from the list of nationally notifiable disease since 1995. According to the Centers for Disease Control and Protection (CDC), cases in the US were commonly found in immigrants from and travellers to endemic countries, people who live in institutions that have poor sanitary conditions and men who have sex with men (10, 19). There was a large-scale outbreak reported in 1933 in a Chicago World's Fair where the water plumbing system was defected that led to contamination of drinking water with sewage. The outbreak resulted in 1,000 cases, with 58 deaths (1).

12. In the UK, this disease is not notifiable and it has been on a decreasing trend in the number of infections in recent years. The number of cases decreased from 214 cases in 2001 to 68 cases in 2008 although the number of cases slightly rebounded in 2009 and 2010 with an annual number of 110 and 105 respectively (Figure 1). Similar to the US, the infection risks are mostly associated with consuming contaminated food or water in endemic countries and men who have sex with men (20).

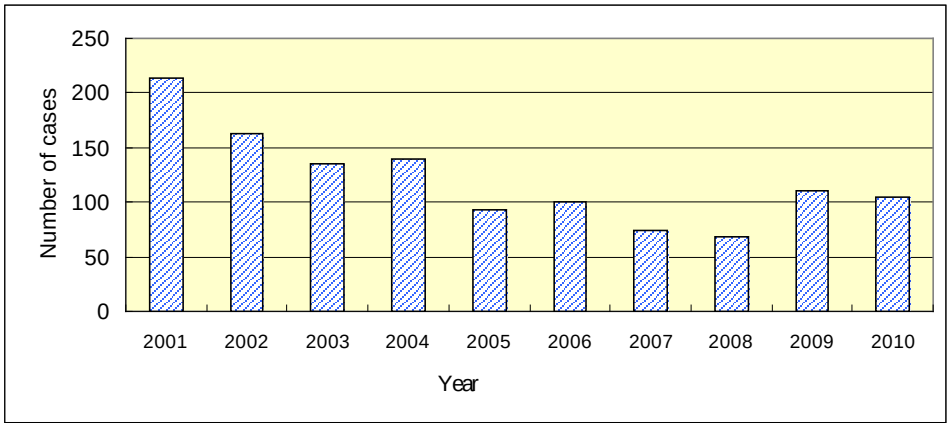

Figure 1.Annual number of *E. histolytica* infection in the UK, 2001 - 2010.

Situations in Central and South America and Asia

13. Amoebic dysentery is a public health concern in the areas of Central and South America as well as Asia. The prevalence varies across areas due to cultural habits, level of sanitation, crowding and socioeconomic status.

Situation in Central and South America

14. In Mexico, people are highly exposed to the *E. histolytica/ E.dispar* infection which was the 6th major cause of disease with incidence of 543.37 cases per 100,000 people in 2007. Serological studies indicated that up to 9% of the population in Mexico City was infected with *E. histolytica*. Children under 15 years of age were susceptible to the infection, especially for the age group between 5-9 years (21, 22).

15. In Brazil, the prevalence of the *E. histolytica/ E.dispar* infection varies across regions, the prevalence was 2.5- 11% in the South and Southeast, 19% in the North/Amazone and approximately 10% in the Northeast and Midwest (23).

Situation in Asia

16. In Malaysia, high prevalence of amoebic dysentery was recorded in tropical highland and mountainous area (21%) and among aborigines population (18.5%) while the prevalence was very low in urban community in Kuala Lumpur (0.4%). This variation was related to the difference in environmental and personal hygiene practices (24).

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17. In Japan, amoebiasis is a notifiable disease. The number of cases increased from 377 cases in 2002 to 747 cases in 2006. Seventy percent of the cases were local cases while the rest were acquired in tropical countries such as Southeast Asia. Mode of transmission was mainly through sexual contact. Outbreaks had been reported among men who have sex with men (MSM) and also residents in institutions for the mentally retarded. In the period between 2003 and 2006, 90% of the cases were males aged 30- 60 years that were 1.7 times increased as compared with those in 1999 - 2002. For the female group, increasing trend was recorded that involved commercial sex workers (CSW). Ten fatal cases were reported in the period of 2003 -2006 (25) .

Local situation

18. Amoebic dysentery is a notifiable disease in Hong Kong. Confirmed case refers to a clinical case that fulfills laboratory criteria with either (i) demonstration of cysts or trophozoites of *E. histolytica* in stool or (ii) demonstration of trophozoites in tissue biopsy or ulcer scrapings by culture or histopathology.

19. As of the end of 2013, there are totally 334 cases recorded since local data is available from 1946. From 1946, the number of cases increased and peaked in 1960. Since then, the number of cases was on a downward trend. The average annual numbers of cases were 39.6 cases, 24.2 cases and 11.1 cases in 70s, 80s and 90s respectively.

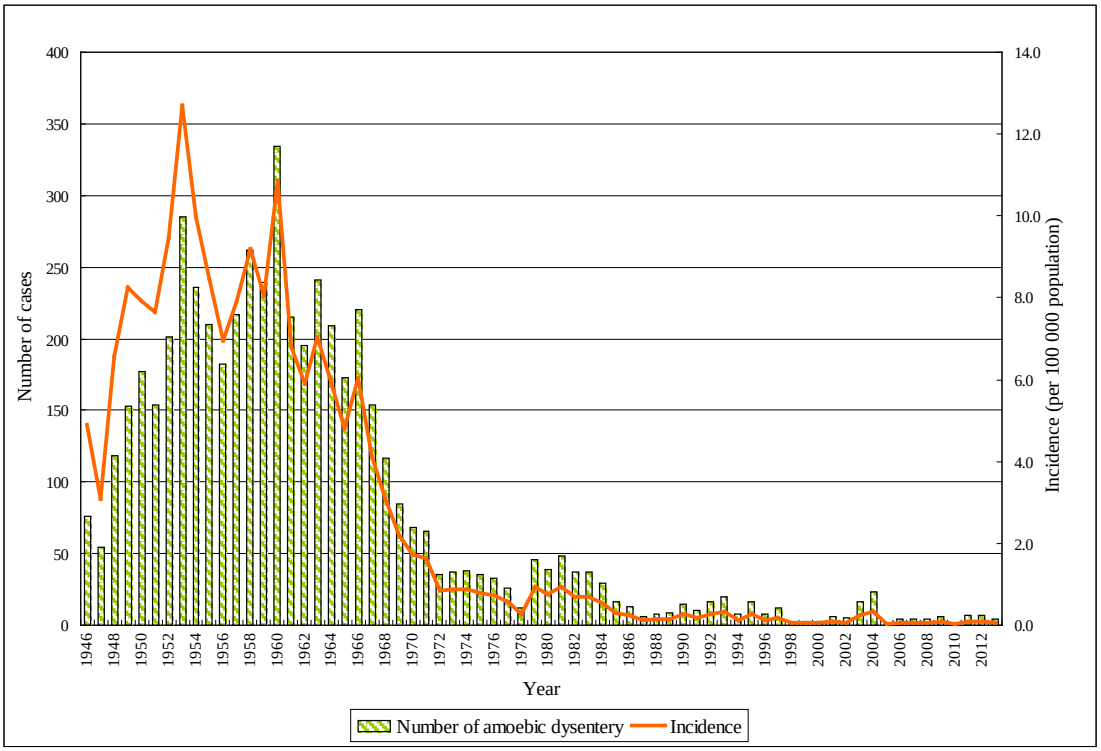

Figure 2 The annual number of cases, incidence of amoebic dysentery in Hong Kong, 1946 – 2013.

20. For the past ten years from 2004 to 2013, the incidence of amoebic dysentery is low in Hong Kong and a total of 63 confirmed cases were reported to the Centre for Health Protection (CHP) of the Department of Health (DH). More cases were reported in 2004 (n= 23, incidence= 0.34 per 100,000 people) while a downward trend was then recorded. There were 2 to 7 cases annually from 2005 to 2013 (median= 4 cases, incidence ranged from 0.03 to 0.1 per 100,000 people) (Figure 3). More male patients were recorded with male-to-female ratio of 2.94:1. The age of patients ranged from 3- 89 years (median= 49 years). More cases (n=30) were observed in the age group between 35- 54 years (Figure 4). Besides, more cases were reported in spring seasons from January to March. No clustering and fatal cases were reported in the past 10 years.

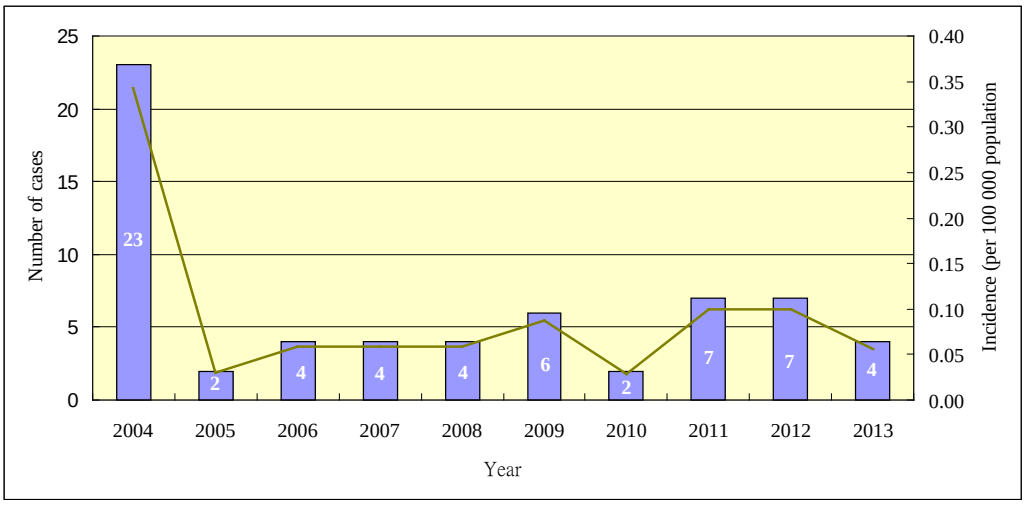

Figure 3 The incidence and the number of confirmed amoebic dysentery in Hong Kong, 2004 – 2013 (n=63)

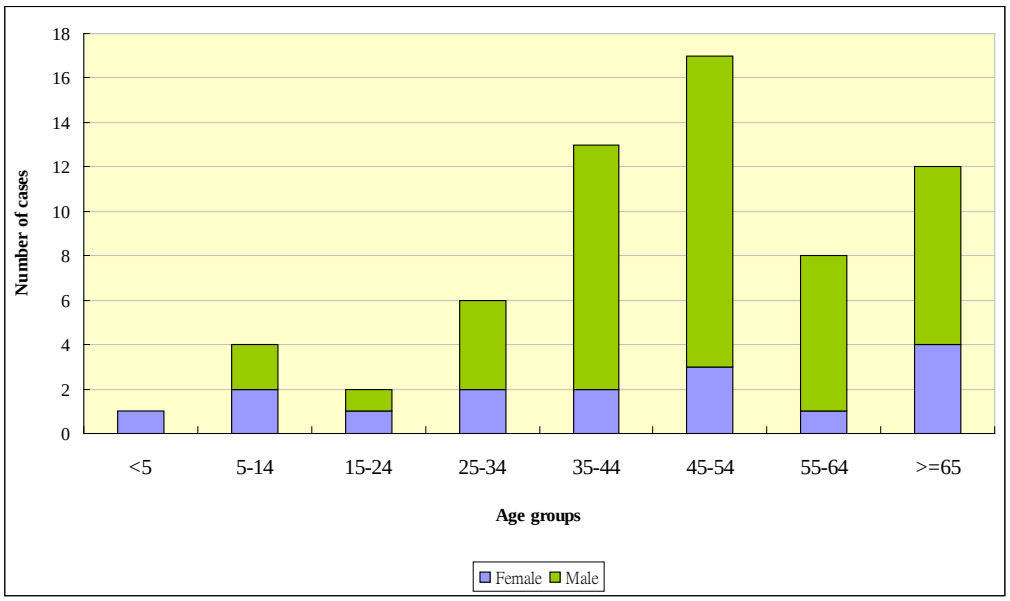

Figure 4 The age and gender distribution of the patients with amoebic dysentery, 2004 - 2013 (n = 63)

21. Among these 63 cases, more than half acquired the disease locally (69.8 %, n=44) while 19.0% (n=12) were imported from various countries including the Mainland China (n= 4), India (n= 2), US (n= 2), Nepal (n= 1), the Philippines (n= 1) and, undetermined (patients stayed in more than one countries) (n=2). Notably, the source of infection of seven cases (11.1%) could not be ascertained as the patients had stayed both locally and overseas during incubation period which is commonly 2-4 weeks. Of these unclassified cases, all of them had travelled histories to Asian countries including Mainland China, India, Indonesia, Japan, the Philippines and Singapore. Three patients were flight attendants and one was a businessman. They all travelled to multiple countries during the incubation period.

22. Sixty five percent of them enjoyed good past health (n= 41). About 62% of them required hospitalisation (n= 39) and the length of stay ranged from 1 to 99 days (median= 4 days). All except one (98.4%, n=62) used main sewerage system and main water supplies. The remaining patient reported to use communal water source. Though the sources of infection could not be ascertained for most cases, a number of known risk factors reported in literature were identified among a proportion of the cases such as drinking well/stream water or unboiled tap water (n=4), consuming raw vegetable in India (n=1), taken cold drink with ice in Thailand (n=1) or being residents of institutions (n=3).

23. Bloody diarrhea (72.6%, n=45) was the most common clinical presentation among the cases. Other symptoms included abdominal pain (62.9%, n=39), mucus in stool (54.8%, n= 34), general diarrhea (41.9%, n= 26) and watery diarrhea (40.3%, n= 25). Thirty seven patients (58.7%) required endoscopic investigation which revealed intestinal ulcers in 33 patients (52.3%). Twenty seven of them required hospitalisation and one required total colectomy. On the other hand, one case of amoebic liver abscess (ALA) was reported and the patient recovered uneventfully after receiving treatment. Approximately 44.4% of the cases (n= 28) were confirmed by direct microscopy in stool specimen with laboratory results of *E. histolytica* cysts/ trophozites (n=15) or *E. histolytica/ dispar* cysts or trophozites (n=13). Fifty six percent (n= 35) were confirmed by histological examination of biopsy specimen with laboratory results of *E. histolytica*.

24. In the past ten years, more than 500 contacts of cases were traced. Five contacts presented with symptoms compatible with amoebic dysentery but faecal specimens were all tested negative for *E. histolytica*. Nevertheless, positive result was recorded for one asymptomatic carrier during contact tracing who was a resident of an institution.

Prevention and control of amoebic dysentery

25. Amoebic dysentery is a food and waterborne disease that can be found worldwide. Effective prevention and control rely on (a) maintaining good environmental sanitation, especially in controlling quality of drinking water; (b) prompt investigation of cases and implementation of control measures to prevent spread of the disease; (c) health education to the general public and food trade on observance of good personal, environmental and food hygiene. The existing prevention and control measures are examined and some potential areas are discussed for further improvement.

Surveillance and control of drinking water quality

26. In Hong Kong, the Water Supplies Department (WSD) is responsible for providing safe and wholesome potable water supply which complies with the World Health Organization's Guidelines for Drinking-water Quality. Through series of chemical and physical processes, raw water is treated to safe drinking water (Diagram 1).

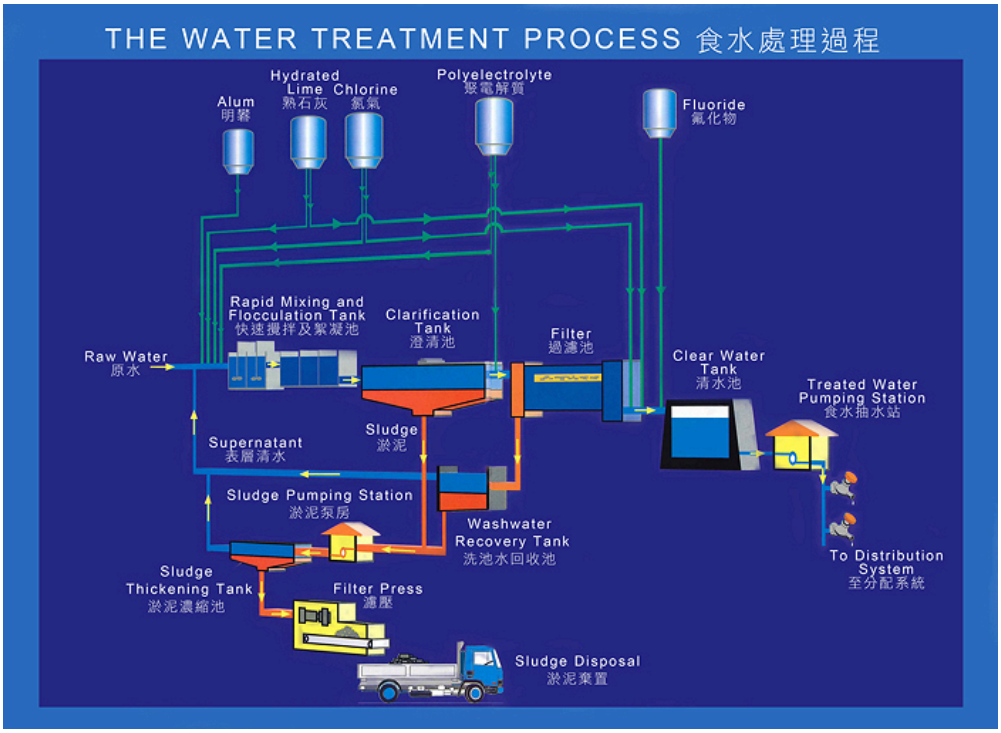

Diagram 1. The water treatment process (Source: Water Supplies Department)

27. The drinking water quality is closely monitored by comprehensive sampling and testing programmes including primary control test at Water Treatment Works, online quality monitoring and regular sampling from the entire water supply system for laboratory testing to ensure safe water supplies. Extensive water samples are collected throughout the water supply system for physical, chemical, bacteriological, biological, radiological and trace substances analyses. Based on the recommendations in World Health Organization's (WHO) "Guidelines for Drinking-water Quality"(2011), WSD adopts a set of health-based guideline values for *Escherichia coli* (*E. coli*) and chemical contaminants and monitors other microbes such as total coliforms, cryptosporidium and giardia which have no health-related guideline value established by WHO to assess the water quality. Regarding the microbiological criteria in a treated water sample, no coliforms and *E. coli* should be found (zero colony forming unit per 100 mL). Besides, oocyst of cryptosporidium and cyst of giardia should not be detected per litre of treated water sample to ensure the microbiological quality of drinking water.

28. WSD provides these monitoring data and compliance status of treated water supply to the Department of Health (DH) on a weekly basis. 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. In the period of October 2012 to September 2013, about 26 000 treated water samples were collected at the water treatment works, service reservoirs, connection points and consumer taps respectively for microbiological testing. All of them complied with the WHO's "Guidelines for Drinking-water Quality (2011)".

29. While about 99.9% of domestic households in Hong Kong are supplied with treated water from WSD, there are some remote villages with sparse population not being covered by the main water supply system. These villagers rely on the raw water systems to supply stream or well water for domestic consumption. Home Affairs Department (HAD) will, upon request from the villagers, repair the water pipes on ad hoc basis and improve the water storage system where necessary. Moreover, the Food and Environmental Hygiene Department (FEHD) regularly monitors and tests the raw water quality to confirm whether the raw water in these villages is suitable for potable consumption. The raw water samples are examined by a series of

suitability tests on turbidity, pH value, odour and colour; chemical analysis on a number of chemical substance such as heavy metal and microbiological tests on total coliform bacteria and *E. coli*. The guideline values recommended by the WHO for drinking water are also applicable to the examination of raw water. With reference to the recommended guideline values, no coliform bacteria and *E. coli* or thermotolerant coliform bacteria should be detected in 100 mL of raw water.

Disease surveillance and public health response

30. Amoebic dysentery is a statutory notifiable disease in Hong Kong. All suspected or confirmed cases will be notified to the Centre for Health Protection (CHP) of DH for prompt investigation and control. CHP initiates investigation immediately upon receiving notification to collect clinical and epidemiological information including history of travel, food consumption and other risk factors such as the mode of water supply and sanitary facilities being used to identify the possible source of transmission. However, known risks like MSM and HIV status are not routinely explored under current practice. Close contacts such as household contacts, food and travel collaterals will also be traced, interviewed to enquire for symptoms and investigated for stool samples. Close contacts or collateral with symptoms of dysentery will also be referred for clinical management.

31. Control measures including education of good personal, food and environmental hygiene to the patients and their close contacts will be given. If indicated, isolation of cases especially for patients with severe symptoms or who are incapable of practicing good personal and food hygiene will be encouraged. All cases will be followed up till they are asymptomatic and have three negative stool specimens collected at least three weeks after completion of treatment with antibiotics. To prevent further spread of the disease, appropriate measures will also be taken to correct the situation when a vehicle or source is identified.

32. Infected food handlers will be ordered to suspend from food-handling work for at least three months after completion of treatment with antibiotics by the FEHD. Health advice on personal hygiene and food safety will be stressed. They can be released from suspension when they have recovered from the disease and there are series of stool specimens found to be negative for the parasites.

Health education to public and travellers

33. Maintenance of good personal hygiene, especially hand hygiene, environmental hygiene and adherence to food and water safety remain the mainstay of prevention of the disease at personal level. FEHD and CHP have prepared a variety of health education materials, such as fact sheets on amoebic dysentery, pamphlets and messages in electronic media on hand hygiene, food and water safety, to increase the awareness of the general public. Furthermore, the website of Travel Health Service of DH is uploaded with the most updated news on infectious disease around the world with relevant health tips available for travellers. However, specific safe drinking-water related health education or health promotional activities targeted to villagers relying on stream or well water is lacking.

Recommendations

34. The trend of amoebic dysentery has been decreasing and there was no clustering of cases reported in Hong Kong in the past 10 years. Although this may be accounted for by the improved sanitation and hygiene practice in Hong Kong as described above, the possibility of under diagnosis cannot be ruled out. Although all of the cases were confirmed by microscopy, *E. histolytica* are morphologically identical with another two non-pathogenic and pathogenicity uncertain Entameoba spp. that cannot be easily differentiated by light microscopy unless *E. histolytica* ingesting red blood cells (erythrophagocystosis) is observed. This would possibly lead to false positive and over-diagnosis. On the other hand, the sensitivity of direct microscopy for diagnosing amoebic colitis is relatively low at below 60% with specificity between 10-50% (2). There are commercially available alternative diagnostic tests which test performance in terms of sensitivity and specificity are reported to be better than microscopy, for example stool antigen test, conventional PCR and real time PCR (26). To assess its applicability in local healthcare setting including both public and private hospitals, further reviews taking into account of the local disease burden, the epidemiology of dysentery due to other pathogens, facilities for proper stool saving and transport, expertise in microscopic examination, relative cost and benefits, etc, are required to be examined. Meanwhile, these alternative tests can be considered for research or in investigation of contacts, where applicable.

35. Besides, the source of transmission could not be ascertained in most of the sporadic cases probably due to the long incubation period of the disease and the under-reporting of certain risk factors in the past during epidemiological investigation (e.g., MSM and HIV status). To fill the information gaps, researches, such as case control studies along with case investigation are encouraged to identify the risk factors and source of infections of amoebic dysentery in Hong Kong. Case investigation protocol to include risk factors e.g. history of MSM and HIV status etc. as part of the routine investigation is also recommended.

36. It is also recommended to keep abreast of the latest development of the availability of luminal agent as there is no registered luminal agent available in Hong Kong and prescription can be made only on named patient basis. .

37. The government is recommended to inform those high risk groups relying on well water and stream waters in Hong Kong about the importance of drinking boiled water if the safety of their water source cannot be confirmed. Travellers to countries or places with poor sanitation should also be informed about the potential risks of drinking untreated water.

Centre for Health Protection
April 2014

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