



衛生防護中心
Centre for Health Protection

Scientific Committee on Enteric Infections and Foodborne Diseases

Review on the Epidemiology and Prevention and Control of Hepatitis A

Purpose

This paper reviews the latest global and local situation of hepatitis A and examines the prevention and control measures of hepatitis A in Hong Kong.

Background

2. Hepatitis A is inflammation of the liver caused by the hepatitis A virus (HAV). It is one of the most frequent causes of foodborne infection. It occurs sporadically and in epidemics worldwide. Every year there are an estimated 1.4 million cases of hepatitis A worldwide.¹ Regions with high HAV endemicity include parts of Africa and Asia.¹ The disease is closely associated with unsafe water, inadequate sanitation and poor personal hygiene.

Clinical features

3. Hepatitis A can cause mild to severe illness. Affected persons of hepatitis A may be asymptomatic. Those who have symptoms may have poor appetite, tiredness, nausea, vomiting, diarrhoea, fever, upper abdominal discomfort, jaundice and tea-coloured urine. The illness may last for a few weeks but may rarely take months to resolve. Infected children under six years of age do not usually experience noticeable symptoms.² Adults have signs and symptoms of illness more often than children, and the severity of disease and mortality increases in older age groups.²



Treatment and prognosis

4. Treatment is mainly supportive and aims at relieving symptoms. Most patients have a complete recovery but in a few cases, the damage to the liver may be prolonged. Hepatitis A infection does not cause chronic liver disease yet it can cause debilitating symptoms and fulminant hepatitis, which is associated with high mortality.² People with chronic liver diseases have increased risk of serious complications if they acquire hepatitis A infection.² Immunity is usually life-long and there is no chronic carrier state.

Incubation period and mode of transmission

5. The incubation period is usually around four weeks but may range from 15 days to 50 days. The HAV is primarily transmitted by the faecal-oral route, that is, when an uninfected person ingests food or water that has been contaminated with HAV. The virus can also be transmitted through close physical contact with an infectious person. Waterborne outbreaks, though infrequent, are usually associated with sewage-contaminated or inadequately treated water.² Since the virus is present in blood during the illness prodrome, HAV has been transmitted on rare occasions by transfusion.³ Viral shedding persists for 1 to 3 weeks. Infected persons are most likely to transmit HAV 1 to 2 weeks before the onset of illness, when HAV concentration in stool is the highest.³ The risk then decreases and is minimal the week after the onset of jaundice.³

6. HAV can be stable in the environment for months. The virus is relatively stable at low pH levels and moderate temperatures but can be inactivated by high temperature (85°C or higher), formalin, and chlorine.³ Bivalve shellfish are filter feeders that absorb food particles and nutrients by filtering out the seawater. They tend to concentrate the virus present in the polluted water. Human may contract hepatitis A after consumption of contaminated shellfish that has not been thoroughly cooked.⁴ Some methods of food preparation such as hotpots and barbecues have higher risk of inadequate cooking. Ready-to-eat food including frozen food, fruit and vegetables may also have higher risk of contamination with HAV in countries where hepatitis A is common and in areas where there are poor sanitary conditions or poor personal hygiene.

Diagnosis

7. Diagnosis of hepatitis A is confirmed by the detection of anti-HAV IgM in the serum of a person with clinically compatible illness. Anti-HAV IgM generally becomes detectable 5-10 days before the onset of symptoms and can persist for up to 6 months.³ During community outbreaks, demonstration of the presence of HAV in stool or serum using reverse transcriptase-PCR technique coupled with nucleotide sequence analysis can help differentiate the genotypes and determine clustering of related cases, which facilitates tracing the source of infection.⁵

Epidemiology

Global situation

8. Geographical distribution areas can be characterised as having different levels of hepatitis A infection.² The World Health Organization (WHO) used 2 main sources of information to estimate the burden of disease associated with hepatitis A infection: (i) serological surveys estimating the prevalence of past infections, and (ii) reporting systems measuring the incidence of morbidity or mortality from acute hepatitis A disease.⁶ WHO classified levels of endemicity on the basis of seroprevalence as high, intermediate, low and very low as shown in Table 1.

HAV endemicity	Seroprevalence	Examples of countries or regions
high	×90% by age 10 years	<ul style="list-style-type: none">● Sub-Saharan Africa● Parts of South Asia
intermediate	×50% by age 15 years, with <90% by age 10 years	<ul style="list-style-type: none">● Asia● Latin America
low	×50% by age 30 years, with <50% by age 15	<ul style="list-style-type: none">● Eastern Europe● Middle East
very low	<50% by age 30 years	<ul style="list-style-type: none">● Western Europe● Australia● New Zealand● Canada● The United States● Japan● Korea● Singapore

Table 1. Examples of countries of different HAV endemicity based on WHO classification

Regions with high HAV endemicity

9. In developing countries with very poor sanitary conditions and hygienic practices, most children (90%) have been infected with HAV before the age of 10. Those infected in childhood do not experience any noticeable symptoms. Epidemics are uncommon because older children and adults are generally immune. Symptomatic disease rates in these areas are low and outbreaks are rare.²

10. Most parts of Africa have very high HAV incidence rate and, correspondingly, a high seroprevalence rate, with most children continuing to develop immunity in early childhood and very few adults at risk of infection.⁷ A 1998 study of urban schoolchildren in Sierra Leone found a 97% prevalence rate.⁷ In these regions, supplies of safe drinking water, proper disposal of sewage and personal hygiene practices would reduce the spread of HAV without a specific vaccination strategy.⁸

Regions with intermediate HAV endemicity

11. In developing countries, countries with transitional economies and regions where sanitary conditions are variable, children often escape infection in early childhood. These improved economic and sanitary conditions may lead to a higher susceptibility in older age groups and higher disease rates, as infections occur in adolescents and adults, and large outbreaks can occur.²

12. In urban China in the early 1990s, one-third to one-half of 10-year olds had antibodies to hepatitis A.⁷ In rural and urban areas in the early 1980s, about half of 5-year-olds had anti-HAV.⁷ The live attenuated hepatitis A vaccine had been available for Chinese children at userø fee since 1992.⁹ The national annual incidence rate of hepatitis A dropped from more than 50 per 100 000 in 1990 to 1992 to about 5 per 100 000 in 2005 to 2006 as the use of hepatitis A vaccine expanded to more than 135 million doses in 2006.⁷ In 2008, hepatitis A immunisation with either live attenuated or inactivated vaccine was recommended for the national routine childhood immunisation programme.⁹ The reported annual incidence rate of hepatitis A kept falling afterwards to 1.82 per 100 000 in 2012.⁹ This reduction in incidence could not be associated with the immunisation programme which had only been run

for 5 years, while the peak incidence were on children aged between 5-14 in the less developed western provinces and on adults in the well-developed eastern provinces.⁹ Therefore, it was deduced that the reduction in hepatitis A incidence was primarily due to rapid urbanisation and improved sanitation in China and secondarily due to immunisation.⁹

Regions with low to very low HAV endemicity

13. In developed countries with good sanitary and hygienic conditions, infection rates are low. Disease may occur among adolescents and adults in high-risk groups, such as injecting-drug users, men who have sex with men, people travelling to areas of high endemicity, and in isolated populations such as closed communities who share common meals prepared with well-water which might be contaminated.² In recent years, hepatitis A outbreaks were documented in countries with low levels of hepatitis A infection.

14. In Europe, there was a multinational hepatitis A outbreak linked to frozen berries in 2013. A total of 331 confirmed cases were reported in Denmark, Finland, France, Germany, Ireland, Norway, the Netherlands, Poland, Sweden and the United Kingdom.¹⁰ Since August 2013, the majority of the cases in the affected countries have been interviewed using questionnaires adapted from the questionnaire initially developed by the Health Protection Surveillance Centre, Ireland.¹⁰ In Italy, Ireland and Norway, case-control studies identified berries and berry products as risk factors. No single point source of contamination could be identified but contamination could be occurring at the freezing processor or in primary production of berries. Contaminated products were recalled and the outbreak in Ireland was declared over in October 2013.¹¹ For the public health domain, the European Food Safety Authority (EFSA) recommended enhanced surveillance, risk communication, vaccination and further research.¹⁰ For surveillance, EFSA and the European Centre for Disease Control and Prevention recommended enhancing epidemiological and microbiological surveillance for HAV, for example, a whole-genome sequencing (WGS) approach should be considered to examine viral isolates from different points in time during an outbreak, which would help to confirm the hypothesis of a single outbreak.¹² HAV vaccination was recommended for (i) close contacts of cases; (ii) non-immune berry-pickers and handlers; and (iii) the larger community, taking into account the epidemiological situation and/or immune status of the local population.¹⁰ Regarding research, EFSA recommended submission of genotyping sequences

to a central database to improve understanding of the ecology of HAV and improve interpretation of genotyping data when applied to outbreak investigations.¹⁰ However, EFSA pointed out that WGS had rarely been used in previous outbreak investigations, and the interpretation of WGS results could be challenging.¹⁰

15. In the United States, there was a multi-state outbreak of hepatitis A illnesses potentially associated with a frozen fruit blend in 2013. 165 people were confirmed to have become ill from hepatitis A linked to pomegranate seeds contained in Townsend Farms Organic Antioxidant Blend in 10 states.¹³ The major outbreak strain of HAV, belonging to genotype 1B, was found in clinical specimens of 117 people in nine states.¹³ This genotype was rarely seen in the Americas but circulated in North Africa and the Middle East. This genotype was identified in the 2013 outbreak of hepatitis A infections in Europe linked to frozen berries and a 2012 outbreak in British Columbia related to a frozen berry blend with pomegranate seeds from Egypt. The Centers for Disease Control and Prevention (CDC) and US Food and Drug Administration (FDA) determined that the most likely vehicle for the HAV appeared to be a common shipment of pomegranate seeds from a company in Turkey.¹³ Products that had the potential to be contaminated with HAV were recalled. The last case of the outbreak was reported in July 2013.¹³

16. In Australia, multiple locally acquired cases of hepatitis A infection have been identified in people who consumed a brand of frozen mixed berries in 2015.¹⁴ As of 25 March 2015, there were 28 cases in six states.¹⁴ All 28 cases reported eating Nanna's frozen mixed berries during their period of acquisition. The product contained raspberries, strawberries and blackberries and blueberries.¹⁴ No other common exposure has been determined. This strong epidemiological association was further strengthened by genotyping. Confirmed outbreak cases have been genotyped as 1a with an identical sequence and this sequence had not been seen previously in Australia (email communication with the Australian Government Department of Health, 1 May 2015). There was no mention of controls. Berries were the only common exposure for all cases but the source of the HAV was unconfirmed. Four products were recalled, namely, one mixed berries product that had been epidemiologically associated with the outbreak and three other products that had been recalled as a precaution.¹⁴

17. For places with low HAV endemicity, HAV outbreaks were effectively contained by identifying the sources of suspected incriminated food and to removing them from the market.

Local situation

18. The Department of Health (DH) has been maintaining a notification system of viral hepatitis since 1974. Since 1988, reported cases have been classified by their viral aetiological agents. In 1992, there was an upsurge of hepatitis A cases affecting more than 3 600 persons. The problem was attributable to the polluted marine environments in the region and the Chinese culinary habits of eating shellfish raw or incompletely cooked.¹⁵ The majority of hepatitis A patients had a history of consumption of bivalves and oysters.¹⁵ Since 1988, except for the major outbreak in 1992, the annual number of hepatitis A cases was observed to have declined from over 1 000 cases in 1988 to less than 100 cases annually in recent years (Figure 1).

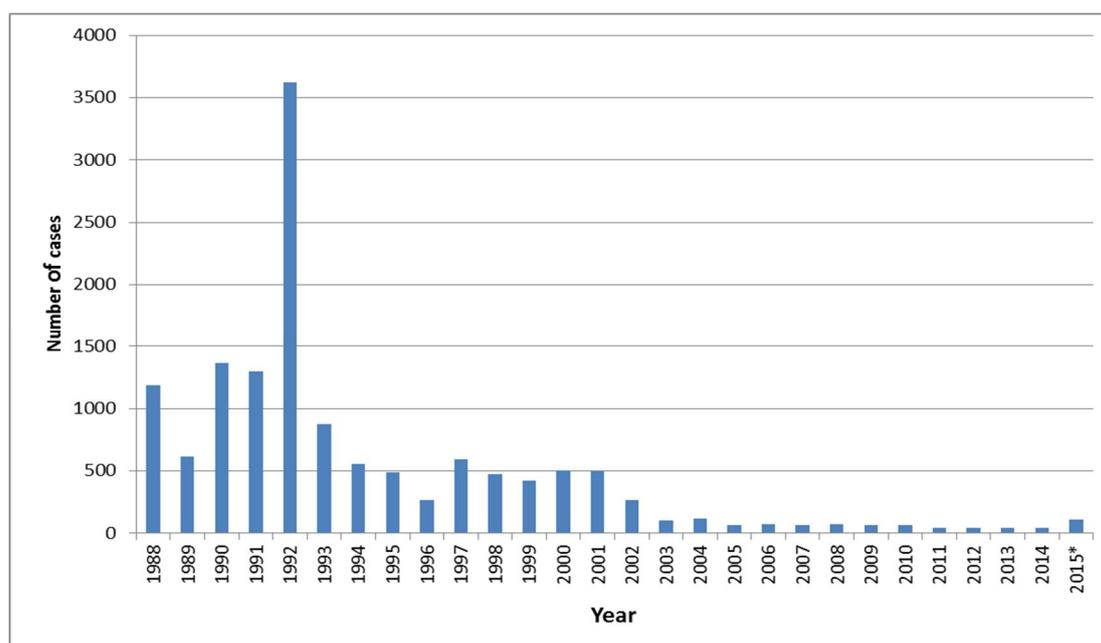


Figure 1. Number of hepatitis A cases by year, 1988 ó 2015 (*as of 30 June 2015)

19. From 2005 to 2014, the number of hepatitis A cases remained relatively stable and the annual number of cases ranged from 43 to 76. In 2015, an increase in the number of cases was observed from February to June, with 109 cases recorded in 2015 (as of June 30) (Figure 2). The number of cases recorded so far in 2015 was the highest compared with those of the

corresponding period in the past 10 years (Figures ranged from 21 to 43 cases from 2005 to 2014).

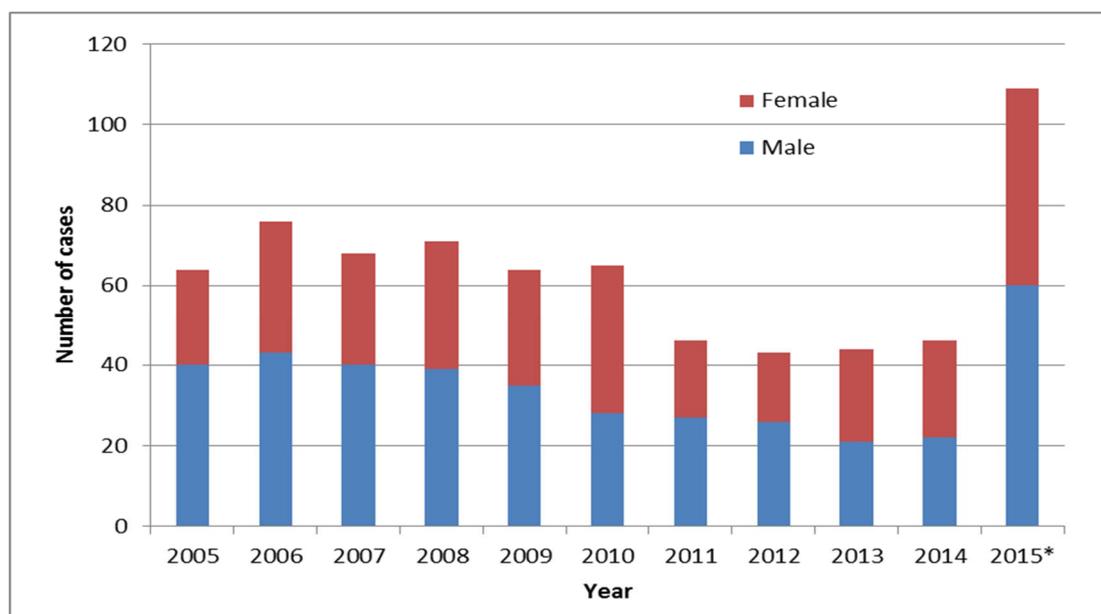


Figure 2. Number of hepatitis A cases by year and sex, 2005 ó 2015 (*as of 30 June 2015)

20. From 2005 to 2014, a total of 587 cases were recorded and the cases occurred throughout the year (Figure 3). The cases involved 321 males and 266 females (male to female ratio = 1.2 : 1), with almost 75% of them aged below 40 years (Figure 4). They commonly presented with tea coloured urine (83%), jaundice (77%), fever (65%), loss of appetite (58%), vomiting (52%), nausea (47%), abdominal pain (42%), muscle pain (34%) and headache (27%). Seventy percent of the patients required hospitalisation, with a median stay of 5ve days. Two fatal cases were recorded, one in 2006 affecting a 78-year-old lady and another one in 2011 affecting a 76-year-old man. Both patients had multiple medical comorbidities.

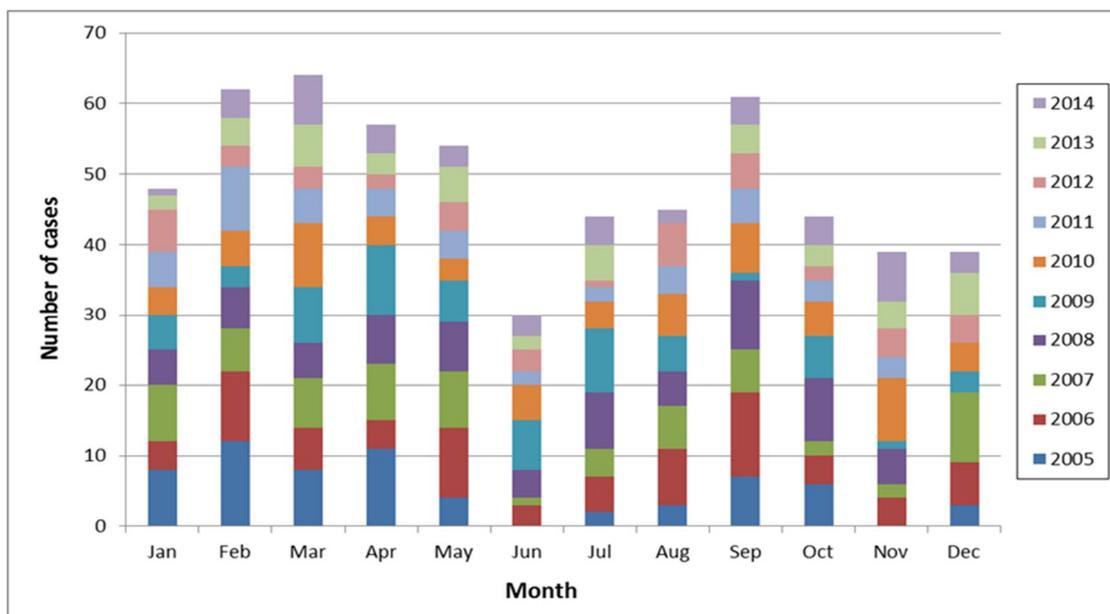


Figure 3. Number of hepatitis A cases by month, 2005 ó 2014

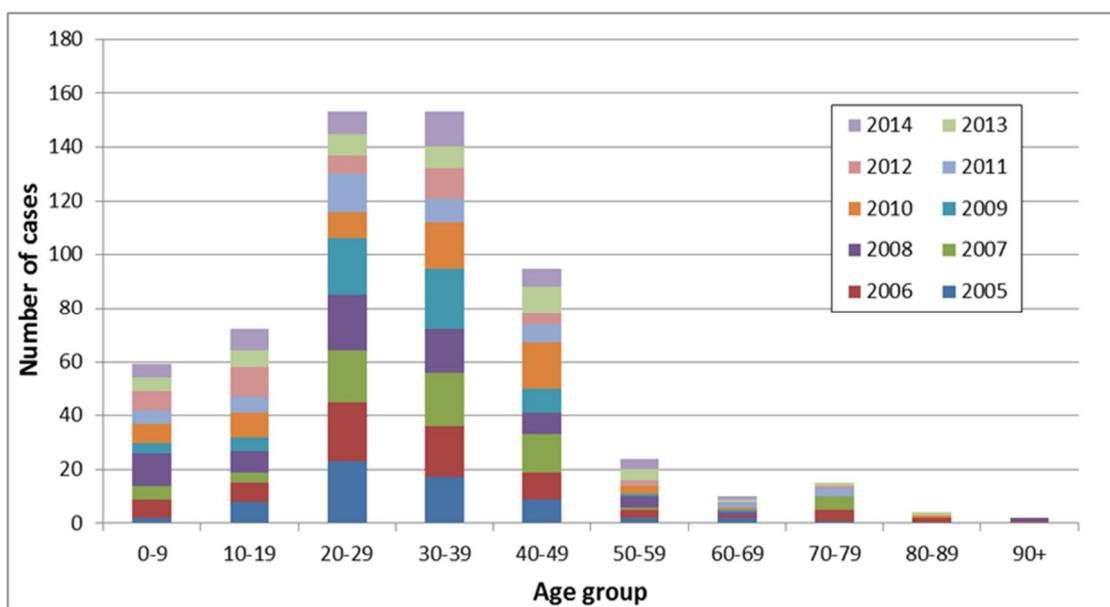


Figure 4. Age distribution of hepatitis A cases, 2005-2014

21. Majority (76%) of the patients acquired the disease locally. Most (92%) of the cases was sporadic infection, whereas 22 small clusters of hepatitis A cases involving two to four patients were also identified. At least 60% of these clusters affected members of same household. Since the incubation period of hepatitis A may range from 15 to 50 days, it is difficult to ascertain the exact source of infection of individual cases.

22. For the 109 cases recorded in 2015 (as of 30 June), 60 males and 49 females were affected (male to female ratio = 1.2 : 1) with age ranging from 3 to 83 years old (median: 33 years old). Most of the cases presented with jaundice and tea-coloured urine. No case required intensive care and there was no fatality. None of the cases could recall any definite history of hepatitis A vaccination. The cases resided in different districts, including 15 in Hong Kong Island, 27 in Kowloon and 67 in the New Territories.

23. The food items consumed and the frequently patronised food stalls were found to be dispersed among the cases. The Public Health Laboratory Services Branch (PHLSB) of the Centre for Health Protection (CHP) has attempted molecular studies on specimens from the cases reported in 2015. In the majority of cases (92%, 55/60) the virus was identified to be of genotype IA and more than 10 genotypically distinct strains were identified among these cases. Forty-three percent of cases (26/60) were found to carry identical hepatitis A sequences. Except two cases from the same family and two cases studying in the same school, no epidemiological link was found among other cases and they were regarded as sporadic cases. So far, no single identifiable source can be found to explain the upsurge of cases in 2015.

Seroprevalence studies

24. Serological surveillance studies on different age groups were performed by the PHLSB of CHP in 2000, 2005 and 2010.¹⁶ The most marked decrease in prevalence of HAV antibodies occurred in the 41-50 age group and there was right-shifting of the age-specific seroprevalence in this and older age groups (Figure 5). The seroprevalence rates showed that HAV endemicity of Hong Kong was very low as defined by WHO.

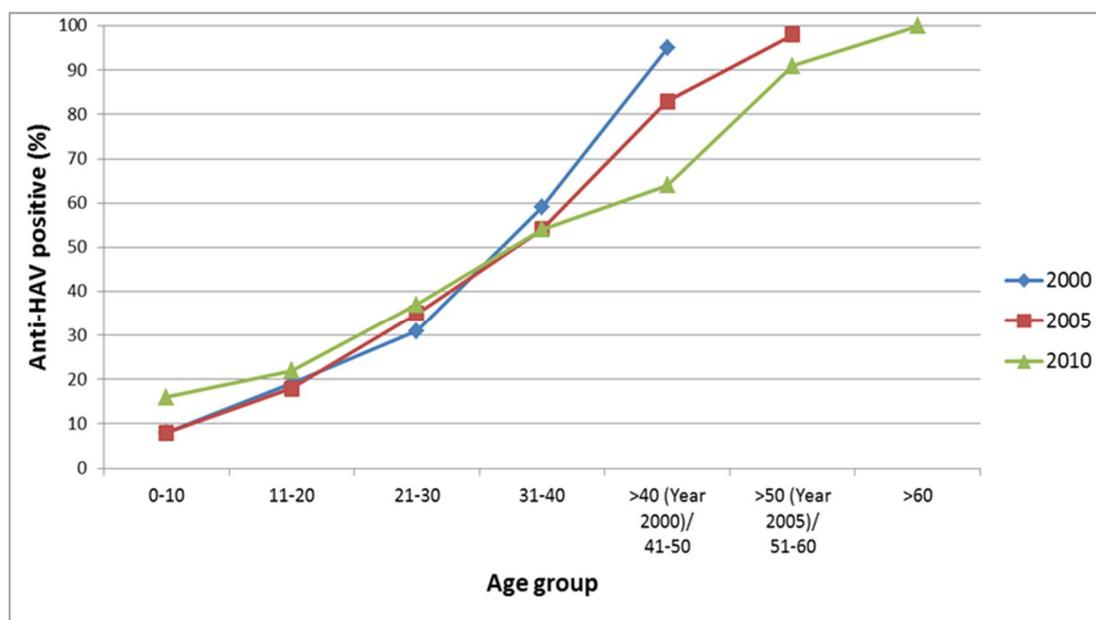


Figure 5. Seroprevalence of hepatitis A in different age groups in 2000, 2005 and 2010.

25. The incidences of hepatitis A of selected countries or regions are listed in Table 2 for comparison. As described in paragraphs 9 and 13, the hepatitis A incidences of regions with high HAV endemicity and regions with low or very low HAV endemicity would both be low. In Hong Kong, the incidence of hepatitis A is low and as reflected by the seroprevalence of hepatitis A, it is a place with very low HAV endemicity.

Country or region	Year of data	Hepatitis A incidence per 100 000 population
Mainland China ^{17,18}	2014 (End-year population was used)	1.9
Australia ¹⁹	2014	1.0
United States ²⁰	2013	0.6
Hong Kong ²¹	2014	0.6
England and Wales ^{22,23}	2014	0.5
Thailand ²⁴	2015 (1 January to 4 August)	0.4
Japan ^{25,26}	2014 (population as at 1 October was used)	0.3

Table 2. Hepatitis A incidence of selected countries or regions (Incidence was either obtained directly from the source, or calculated using mid-year population of the corresponding year unless otherwise stated)

Hepatitis E

26. As hepatitis E is also transmitted by the faecal-oral route, the annual number of hepatitis A and hepatitis E cases is presented in Figure 6 for comparison. Since 1996, the annual number of hepatitis E cases has increased steadily from 11 in 1996 to 150 in 2012, and then decreased to 93 in 2014. There was no association between the number of hepatitis A and hepatitis E cases in Hong Kong over the past 20 years.

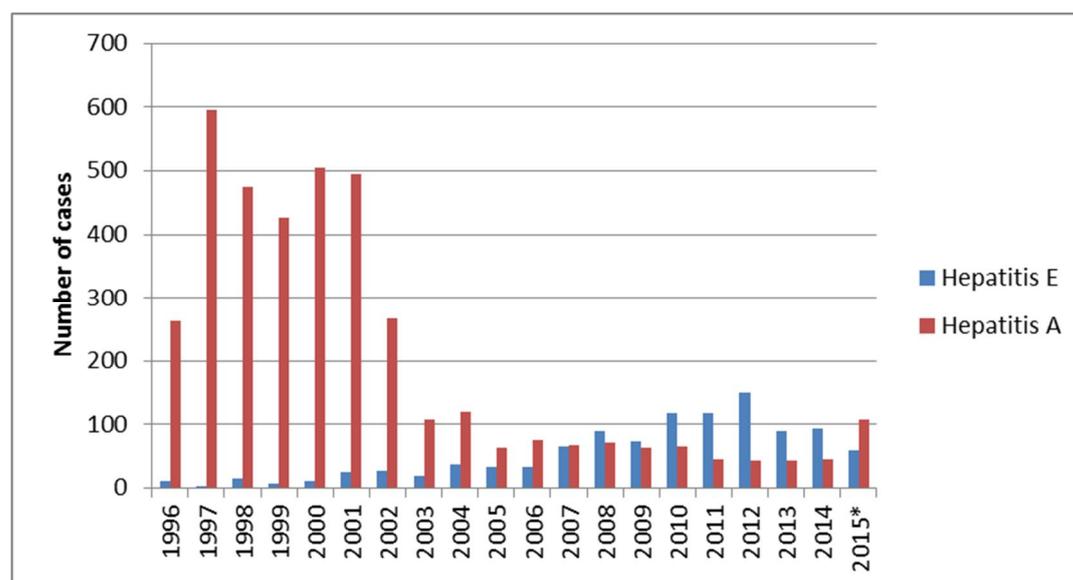


Figure 6. Number of hepatitis A and hepatitis E cases by year, 1996 ó 2015 (*as of 30 June 2015)

Prevention and Control

27. In the absence of specific treatment, WHO recommends a preventive approach to hepatitis A encompassing the following components:

- Providing safe drinking water and proper disposal of sanitary waste;
- Food safety;
- Vaccination;
- Personal hygiene practices;
- Monitoring disease incidence;
- Detecting outbreaks;

- Determining sources of infection; and
- Containing spread.^{1,2}

Water quality and sewerage

28. Hong Kong has well-developed systems in place to provide clean water and good sanitation conditions to the public. In Hong Kong, the Water Supplies Department supplies safe drinking water which quality fully conforms to the Guidelines for Drinking-water Quality recommended by the WHO.²⁷ The Drainage Services Department provides wastewater and stormwater drainage services. About 93% of the Hong Kong population are served by the public sewerage system.²⁸ In rural areas not served by public sewers, private developers need to provide their own sewage treatment facilities according to guidelines set out by the Environmental Protection Department.²⁹

Food safety

29. In Hong Kong, the Centre for Food Safety (CFS) of the Food and Environmental Hygiene Department (FEHD) is responsible for enforcement of food safety legislation and import control. Under the Public Health and Municipal Services Ordinance, Cap.132, all food intended for human consumption, locally produced or imported, should be fit for human consumption.³⁰ Members of the food trade should ensure that food intended for sale and human consumption is fit for human consumption.

30. In addition, the Food Safety Ordinance, Cap. 612, provides new food safety control measures, including a registration scheme for food importers and food distributors and a requirement for food traders to maintain proper records of the movements of food to enhance food traceability.³¹ It also empowers the authorities to make regulations for tightening import control on specific food types and to make orders to prohibit the import and supply of problem food and order the recall of such food.³¹ Should the need of recalling food contaminated with HAV arises, relevant authorities in Hong Kong are empowered by this ordinance to trace and recall the food products.

31. Under the Public Health and Municipal Services Ordinance, Cap.132, importers are encouraged to obtain health certificates issued by health authorities of the countries of origin certifying that each imported consignment of shellfish is fit for human consumption. When a consignment of shellfish arrives at entry points, it may be subject to inspection or sampling by FEHD.⁴

32. Codex and food safety regulatory authorities across the world have adopted the view that routine testing for viruses in food is of limited use because (i) the virus in contaminated food is usually present at such low levels that the pathogen cannot be detected by available analytical methods; (ii) the virus can be unevenly distributed and a test result may be negative but the food is still unsafe; and (iii) a positive test result can be due to the presence of genomic material from inactive or non-infectious virus in the food, but this does not mean the virus is active.³²

Outbreak investigation and control

33. In Hong Kong, mechanism is in place to keep surveillance on hepatitis A. All registered medical practitioners are required to report suspected or confirmed cases of viral hepatitis to the CHP. Upon receipt of notifications, the CHP would carry out investigation and public health control measures. Cases are defined as persons with compatible clinical features together with either the presence of anti-HAV IgM antibody or being epidemiologically linked with another laboratory confirmed hepatitis A case.

34. The patient and his attending physician would be interviewed for relevant clinical information. Detailed food, travel, and vaccination history and risk factors would be elicited. Food collaterals, travel collaterals and household contacts would also be traced and kept on medical surveillance. When a common food source is identified or suspected, FEHD would be informed for further investigation and control of the food source. In institutional outbreaks, field visits would be carried out to search for common source of infection and instigation of control measures.

35. In response to the upsurge of hepatitis A cases in 2015, the CHP used a revised questionnaire to capture a wide range of exposures in order to explore possible risk factors of infection. In-depth food history was taken from the index cases to investigation the source of incriminated food. Epidemiological investigations so far could not identify any source and epidemiological linkages among the cases.

Public education

36. DH and FEHD contribute to public education on the prevention of hepatitis A. Since hepatitis A infection is transmitted through the faecal-oral route, promoting good personal, food and environmental hygiene is of importance in preventing infection. The CFS promotes the practising of the 'Five Keys to Food Safety' to prevent foodborne hepatitis A infection:

- Choose (Choose safe raw materials);
- Clean (Keep hands and utensils clean);
- Separate (Separate raw and cooked food);
- Cook (Cook thoroughly); and
- Safe Temperature (Keep food at safe temperature).³²

Vaccine

37. Both active and passive immunisations are effective in preventing and controlling hepatitis A infection. Passive immunisation with human immunoglobulin is effective in providing short term (1 to 2 months) and long term (3 to 5 months) pre-exposure prophylaxis and is effective for post-exposure prophylaxis if given within 14 days of exposure. Persons who have received a dose of hepatitis A vaccine at least 2 weeks before exposure to HAV do not need immunoglobulin.³³ Currently, there are several inactivated vaccines licensed and commercially available for active immunisation against hepatitis A. The vaccines are given parenterally as a 2-dose series, 6 to 18 months apart. In Hong Kong, none of the vaccines are licensed for use in those younger than one year. A combined vaccine for hepatitis A and hepatitis B is also available.³³

38. In 2006, the Scientific Committee on Vaccine Preventable Diseases, CHP, recommended the following groups to have hepatitis A vaccination as pre-exposure prophylaxis for personal protection:

- Persons with chronic liver disease;
- Persons with clotting factors disorders receiving plasma-derived replacement clotting factors; and
- Travelers to endemic areas.³³

39. Depending on the epidemiological profile and setting of the outbreak, post-exposure prophylaxis can be recommended when a hepatitis A outbreak occurs in a closed institution. Either hepatitis A vaccine or immunoglobulin can be considered as appropriate to the outbreak situation. A

number of health authorities have updated their guidelines on post-exposure prophylaxis of hepatitis A to recommend hepatitis A vaccine or immunoglobulin as post-exposure prophylaxis.

40. Recommendations on immunisation for hepatitis A by WHO and different overseas countries are summarised in Annex 1. In Hong Kong, a cost-benefit analysis of hepatitis A vaccination of infants was conducted from 2006 to 2008. It showed that, given the low incidence of hepatitis A in Hong Kong, hepatitis A vaccine would have a very high cost per life year saved, and hence hepatitis A vaccination of infants in Hong Kong as pre-exposure prophylaxis would have no cost-benefit advantage at that time.³⁹

Recommendations

41. With development of advanced water systems and sewerage over the past few decades, Hong Kong had moved from being a hepatitis A endemic area to an area of very low endemicity. The well-developed water and sewerage systems suggested that transmission of hepatitis A by contaminated water was unlikely in Hong Kong. On the other hand, foodborne hepatitis A outbreaks were seen in developed countries in recent decade. These outbreaks were contained by epidemiological investigation, source identification and food safety control measures that are already have mechanism in place in Hong Kong. To further enhance the prevention and control of hepatitis A, the following recommendations are made:-

Epidemiological investigation

42. Disease reporting is still important in identifying affected patients and initiation of investigation for potential outbreaks. Epidemiological investigations should focus on identifying the source of infection and eliciting risk factors for spread. As the incubation period of hepatitis A is long and the high risk food consumed during this long period are usually popular among both the patients and the non-affected persons, it is difficult to identify the incriminated food without comparison with appropriate control groups. Appropriate study designs such as case-control studies are encouraged in the epidemiological investigation of hepatitis A outbreaks.

Risk communication

43. Effective risk communication should be maintained with overseas health authorities, members of the food trade and the public. Alertness to foodborne hepatitis A outbreaks in countries which may import food to Hong Kong should be maintained. Risks of hepatitis A should be publicised through various channels to members of the food trade and the public to raise their awareness on food and personal hygiene and proper preventive measures.

Review vaccination strategy

44. As the previous economic evaluation on hepatitis A vaccine was conducted in the 2000s, an updated economic evaluation could be considered. As a number of health authorities have updated their guidelines on post-exposure prophylaxis, it might be of value to review the local guidelines on post-exposure prophylaxis on hepatitis A or for specific target groups.

Centre for Health Protection

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Annex 1 Recommendation on hepatitis A vaccination among different authorities and countries

Authority/ Country	Recommendation on hepatitis A vaccination as pre-exposure prophylaxis	Recommendation on hepatitis A vaccination as post-exposure prophylaxis
WHO ⁶	<p>Highly endemic countries - Large-scale vaccination programmes are not recommended.</p> <p>Countries with improving socioeconomic status - Large-scale hepatitis A vaccination is likely to be cost-effective and is therefore encouraged.</p> <p>Countries with low and very low endemicity - Targeted vaccination of high-risk groups should be considered. Groups at increased risk of hepatitis A include travelers to areas of intermediate or high endemicity, those requiring life-long treatment with blood products, men who have sex with men, workers in contact with non-human primates and injection drug users. Patients with chronic liver disease are at increased risk for fulminant hepatitis A and should be vaccinated.</p>	<p>The use of hepatitis A vaccine rather than passive prophylaxis with immune globulin should be considered for pre-exposure prophylaxis (e.g. for travellers to areas of higher hepatitis A endemicity) and post-exposure prophylaxis (e.g. for close contacts of acute cases of hepatitis A).</p>
United States ^{3,34}	<p>Hepatitis A vaccine is recommended for all children at age 1 year.</p> <p>For persons aged 1 year and older, vaccine is recommended for the following:</p>	<p>Persons who recently have been exposed to HAV and who previously have not received hepatitis A vaccine should be administered a single dose of single-antigen hepatitis A vaccine or immunoglobulin (0.02 mL/kg) as</p>

	<ul style="list-style-type: none"> • people who live in a community with a high rate of hepatitis A • men who have sex with other men • people who use street drugs • people who work or travel to countries with high rates of hepatitis A • people who have long-term liver disease • people who receive blood products to help their blood clot • people who work with HAV-infected animals or work with HAV in research setting 	<p>soon as possible.</p> <ul style="list-style-type: none"> • For healthy persons aged 12 months to 40 years, single-antigen hepatitis A vaccine at the age-appropriate dose is preferred. • For persons aged >40 years, immunoglobulin is preferred; vaccine can be used if immunoglobulin cannot be obtained. • For children aged <12 months, immunocompromised persons, persons who have had chronic liver disease diagnosed, and persons for whom vaccine is contraindicated, immunoglobulin should be used.
<p>United Kingdom^{35,36}</p>	<p>Vaccination against hepatitis A is recommended for people who:</p> <ul style="list-style-type: none"> • are planning to travel to or live in parts of the world where hepatitis A is widespread, particularly if levels of sanitation and food hygiene are expected to be poor • have any type of long-term (chronic) liver disease • have haemophilia (a blood disorder than can affect the ability of blood to clot properly) • are a man who has sex with other men 	<p>Household or sexual contacts seen within 14 days of exposure to index case</p> <ul style="list-style-type: none"> • Healthy contact aged 1-50 years - Offer hepatitis A vaccine. • Healthy contact aged 2-12 months - Vaccinate carers to prevent tertiary infection OR offer hepatitis A vaccine to the infant (unlicensed) OR exclude from childcare. • Healthy contact aged under 2 months - Offer vaccination to carers to prevent tertiary infection. • Contact aged 50 years or over, or with chronic

	<ul style="list-style-type: none"> • regularly inject illegal drugs • work with or near sewage (untreated sewage is often contaminated by hepatitis A) • work in institutions where levels of personal hygiene may be poor, such as a homeless shelter • work with primates (monkeys, apes, baboons, chimps, gorillas) as these can also be infected with hepatitis A 	<p>liver disease or chronic hepatitis B or C infection - Offer hepatitis A vaccine + human normal immunoglobulin (HNIG).</p> <p>Household or sexual contacts seen more than 14 days post exposure</p> <ul style="list-style-type: none"> • More than one contact within the household and contacts seen within 8 weeks of exposure - Offer hepatitis A vaccine to prevent tertiary infection. • Contact has chronic liver disease or chronic hepatitis B or C infection and is seen within 28 days of exposure - Offer hepatitis A vaccine + HNIG to try to attenuate severity of disease.
Australia ³⁷	<p>Hepatitis A vaccination is recommended for the following groups:</p> <ul style="list-style-type: none"> • Aboriginal and Torres Strait Islander children residing in the Northern Territory, Queensland, South Australia and Western Australia • travelers (×1 year of age) to hepatitis A endemic areas • persons whose occupation puts them at increased risk of acquiring hepatitis A • persons whose lifestyle puts them at increased risk of acquiring hepatitis A 	<p>Post-exposure prophylaxis using hepatitis A vaccine or HNIG can be used to prevent secondary cases in close contacts of hepatitis A cases. However, vaccination is recommended in preference to HNIG for use in post-exposure prophylaxis in persons ×12 months of age who are immunocompetent.</p>

	<ul style="list-style-type: none"> • persons with developmental disabilities • persons with chronic liver disease, liver solid organ transplant recipients and/or those chronically infected with either hepatitis B or hepatitis C viruses 	
Canada ³⁸	<p>Recommended recipients of hepatitis A vaccine for pre-exposure prevention:</p> <ul style="list-style-type: none"> • Travelers to or immigrants from hepatitis A endemic areas • Household or close contacts of children adopted from hepatitis A endemic countries • Populations or communities at risk of hepatitis A outbreaks or in which hepatitis A is highly endemic (e.g., some aboriginal communities) • Persons with lifestyle risks for infection, including those who use illicit drugs (injectable and non-injectable) and men who have sex with men (MSM) • Persons who have chronic liver disease from any cause, including persons infected with hepatitis B or C. While these persons may not be at increased risk of hepatitis A infection, they may be at risk of more severe disease if infection occurs • People with hemophilia A or B receiving plasma-derived replacement clotting factors 	<p>Post-exposure prophylaxis should be offered to household and close contacts of proven or suspected cases of hepatitis A. It should be given when hepatitis A occurs in group child care centres and kindergartens, and should be offered to co-workers and clients of infected food handlers. Post-exposure prophylaxis is not necessary for other contacts, such as school, workplace or health care workers caring for hepatitis A cases, unless an outbreak is suspected.</p> <p>Hepatitis A vaccine is effective as post-exposure prophylaxis to prevent infection in contacts and is recommended in preference to immunoglobulin for people over one year of age. One dose of hepatitis A vaccine should be given to susceptible contacts as soon as possible and preferably within 14 days of last exposure. However, hepatitis A vaccine should still be considered if more than 14 days have elapsed since last exposure, as there are no data on the outer limit of efficacy.</p>

	<ul style="list-style-type: none"> • Military personnel and humanitarian relief workers likely to be posted to areas with high rates of hepatitis A • Zoo-keepers, veterinarians and researchers who handle non-human primates • Workers involved in research on HAV or production of hepatitis A vaccine who may be exposed to HA virus • Any person who wishes to decrease his or her risk of hepatitis A 	<p>Immunoglobulin is the recommended post-exposure immunoprophylactic agent for infants less than one year of age, for those for whom vaccine is contraindicated, and if hepatitis A vaccine is unavailable. Immunocompromised people should receive immunoglobulin in addition to hepatitis A vaccine because they may not respond fully to the vaccine. For post-exposure prophylaxis, the dose of immunoglobulin is usually 0.02 mL/kg, given as soon as possible after an exposure. Efficacy of immunoglobulin is unknown if more than 14 days have elapsed since the last exposure.</p>
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