衞生防護中心
Centre for Health Protection

Scientific Committee on Enteric Infections and Foodborne Diseases

Changing Epidemiology of Hepatitis A in Hong Kong and Implications on Control Strategies

Purpose

Hepatitis A has a worldwide distribution, and is a classic example of an infectious disease with an epidemiological pattern that closely relates to the level of socioeconomic development. As disease incidence continues to fall with economic development and improvement in living conditions, there is need for individual countries to periodically reassess the risk of hepatitis A to guide public health actions against the disease.

2. At the 5th meeting of the Scientific Committee (SC) held on 15 September 2005, Members discussed on the broad strategies for the prevention and control of hepatitis in Hong Kong and agreed to set up a Working Group to develop specific recommendations.

3. The Working Group on the Prevention and Control of Hepatitis A (WGHEPA) was subsequently formed and met on 23 February 2006 to deliberate on the specific recommendations. A further joint meeting of the WGHEPA with the Working Group on Hepatitis formed by the Scientific Committee on Vaccine Preventable Diseases was conducted on 12 May 2006. This paper reviews the changing epidemiology of hepatitis A in Hong Kong, and outlines the prevention and control measures proposed by the WG in response to these changes.

The disease

4. Hepatitis A is an inflammatory disease of the liver caused by the Hepatitis A virus (HAV). HAV is a non-enveloped, single stranded RNA virus which belongs to the picornavirus family; genus Hepatovirus, which was first identified by electron microscopy in 1973.

Clinical features

5. Human is the only reservoir of HAV. The virus targets primarily hepatocytes. It has no cytolytic activity, but the cell mediated response causes damage to the liver. The disease is usually self-limiting but varies in clinical severity from a mild illness lasting 1 to 2 weeks to a severe disease lasting several months. Onset of illness is abrupt and symptoms may include fever, malaise, nausea, anorexia, abdominal discomfort, dark urine, and jaundice.

6. The likelihood of developing a clinical illness and the severity of hepatitis A increases with age. Around 10% of children aged 6 years or younger are symptomatic whereas over 70% of adults become symptomatic. This characteristic contributes to the efficient spread of the virus from asymptomatic young children to other children and to adult contacts. Young children are thus considered to be a principal reservoir and dominant source of transmission in the community[1].

Treatment and Prognosis

7. Treatment is mainly supportive and aims at maintaining comfort and adequate nutritional balance. Complete recovery is generally the rule. Prolonged or relapsing symptoms over 6 to 9 months may occur in 10% to 15% of acute hepatitis A infections but chronic infection has not been documented[2,3,4,5]. Reported case-fatality is low, between 0.1% and 0.3%, and the case-fatality increases with age. Mortality is higher in persons with chronic liver disease, or those co-infected with hepatitis B or hepatitis C, or in elderly[6,7]. During the large outbreak of hepatitis A associated with the consumption of raw clams in Shanghai in 1988, the fatality rate observed among patients with chronic hepatitis B (0.05%) was 5.6 times the rate among those without background hepatitis B infection (0.009%)[8]. HAV has only one known serotype and infection induces livelong immunity against re-infection[9].

Incubation period and mode of transmission

8. The incubation period of hepatitis A averages between 28 and 30 days, although it can range from 15 to 50 days. Virus shedding in stools at high titres begins 3 to 10 days prior to onset of illness, and may continue till 1 to 2 weeks after the onset of jaundice[3,10.]

9. The disease is primarily transmitted via consumption of contaminated water or food such as raw or inadequately cooked mollusk-like oysters and clams harvested from contaminated water. On the other hand, person-to-person spread is more common among those living in close institutions. On rare occasions, HAV can be transmitted by transfusion of blood or blood products[2].

Laboratory diagnosis

10. Diagnosis of hepatitis A is confirmed by the detection of anti-HAV IgM in the serum of a person with clinically compatible symptoms. Anti-HAV IgM becomes detectable about 3 weeks after exposure. The titre increases over 4 to 6 weeks followed by a decline to non-detectable levels generally within 6 months of infection.

11. Detection of total immunoglobins or IgG antibodies in the serum in the absence of IgM antibodies usually signifies past infection. Although HAV is present in the stool in the presymptomatic and early stages of illness, viral cultures are not generally done because of the difficulty in isolating the virus in tissue cultures[4,10].

HAV in the environment

12. HAV is stable in the environment that allows its maintenance and spread within populations. Heating foods to temperatures of 85ºC for 1 minute or disinfecting surfaces with a 1:100 dilution of sodium hypochlorite is necessary to inactivate the virus. Shellfish from contaminated areas should be heated to 90ºC for 4 minutes or steamed for 90 seconds for inactivation of the virus[2,9].

Endemicity and disease pattern

13. Worldwide, an estimated 1.5 million clinical cases of hepatitis occur each year. The epidemiology of hepatitis A infections varies greatly among different countries and populations. Prevalence of anti-HAV antibodies has been found to vary from 15% to 100% in different parts of the world. Geographic areas can be characterized by their age-specific seroprevalence rates into patterns of high, intermediate, and low endemicity. The patterns of endemicity of HAV has been found to be closely related to socioeconomic development[4,11,12.]

14. In the high endemicity areas, over 90% of children may be infected by the age of 5 while reported disease incidence may vary from 1 to 40 per 100,000 per year. Examples are countries in Africa, parts of Asia and Latin America, where overcrowding is common and both hygienic and sanitary conditions are poor. In these areas where infections with HAV occur at a very

young age, clinical hepatitis A and outbreaks are uncommon as most adults are asymptomatically infected during childhood[9,12,13.]

15. In areas with intermediate endemicity, the prevalence of antibody against hepatitis A in children under the age of 10 is low and the major increase in antibody occurs in adolescence and early adulthood[4]. However, as the disease is more likely to be symptomatic in adults, there are generally more clinical cases reported in these areas. This pattern is usually seen in the developing countries and countries with transitional economies, such as those in Southern and Eastern Europe, and some regions in the Middle East[9]. Hepatitis A may represent a substantial medical and economic burden in these areas where a paradoxically higher disease incidence is seen despite improved economic and sanitary conditions.

16. In areas with low endemicity, hepatitis A infection often occur in adolescents and adults in high-risk groups, such as travelers to areas of high or intermediate endemicity. Examples are Australia and the United States of America (USA), Northern and Western Europe, Japan, New Zealand, and Canada. Disease incidence is low and cases occur sporadically or as outbreaks involving a small number of persons.

17. Epidemiological studies and disease surveillance in intermediate and low endemicity countries have identified common risk factors of hepatitis A infection to include[1,13] :

(a) Household or sexual contact with a person with hepatitis A;
(b) History of injection-drug use within 6 months before onset of illness;
(c) Attendance or employment at day care centres and institutions;
(d) A history of male homosexual activity within the prior 6 months; and
(e) Recent international travel to hepatitis A endemic countries.

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. The Scientific Working Group on Viral Hepatitis Prevention of Department of Health, constituted by professionals in microbiology, public health, and clinical fields from government departments, academic institutions and public hospitals, regularly reviewed reports from different studies for local seroprevalence data on viral hepatitis (Appendix 1). We examined these local data to determine the changes in the local epidemiology.

Disease notification

19. There has been continued reduction in the disease incidence of hepatitis A in recent years. Between 1989 and 2004, the annual number of

hepatitis A cases ranged from 107 to 3626 (Figure 1). An upsurge of cases occurred in 1992 with a notification rate reaching 63 per 100,000 population, affecting mostly the 10 to 29 age group while only 0.4% occurred in those aged 50 or above[14].

20. Since then, a gradual declining trend in overall incidence has been observed. The incidence rates were 1.57 in 100,000 in 2003 and 1.72 in 100,000 in 2004. As for the seasonal pattern, cases were more commonly reported between January and May each year (Figure 2).

Figure 1 Notification rates and death rates of hepatitis A, 1989 – 2004

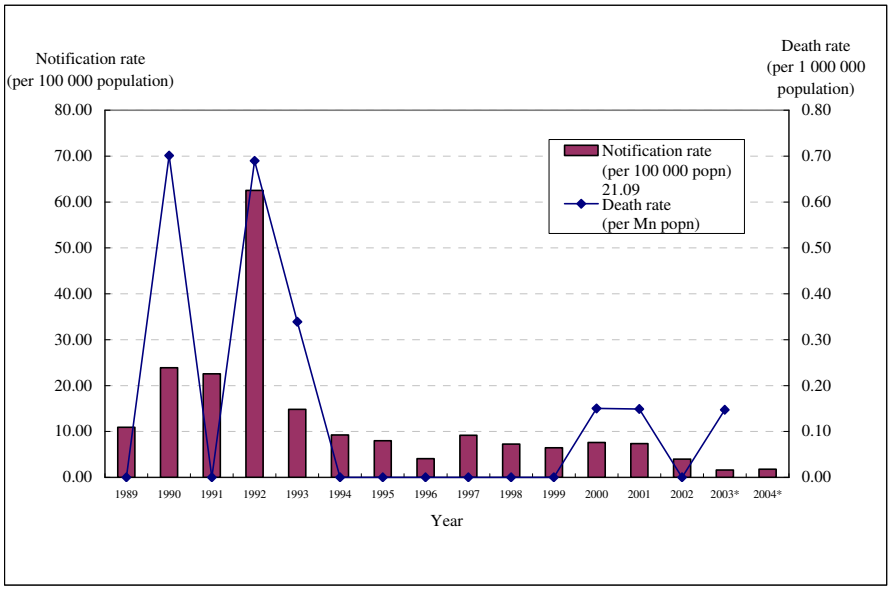
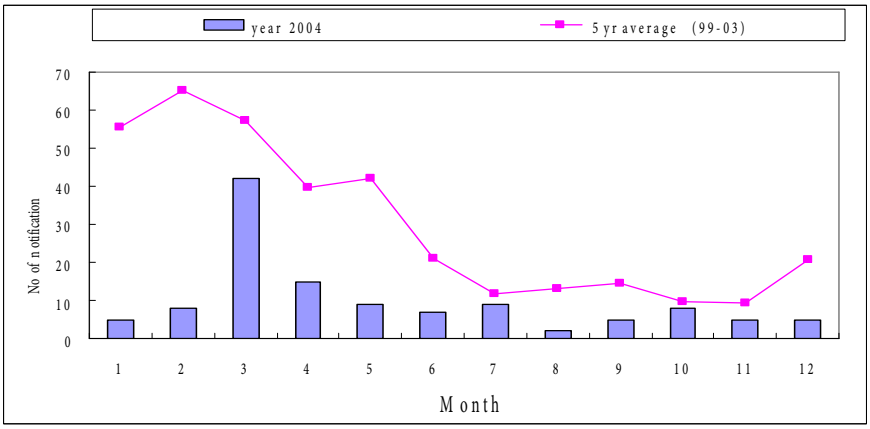


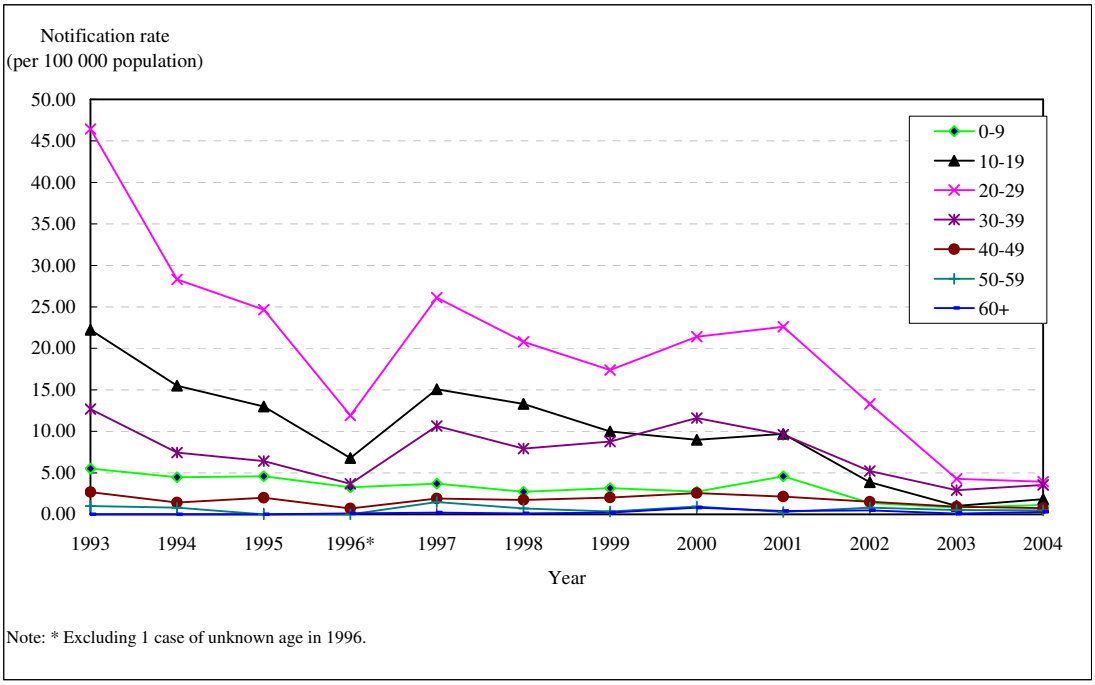
Figure 2 Monthly distribution of hepatitis A , 1999-2004



Age distribution of cases

21. The drop in disease notification rate is most obvious in the 20-29 and the 10-19 age groups (Figure 3). There is an overall increase in the median age of the notified cases from 23 years in 1989 to 29.5 years in 2004 with an increase in the proportion of cases among the 30-39 age group.

Figure 3 Age-specific notification rates of hepatitis A, 1993-2004



Note: * Excluding 1 case of unknown age in 1996.

Outbreaks and risk factors

22. The largest outbreak of hepatitis A recorded most recently was in 1999 when 28 residents and 10 staff of a mental hospital were affected by person-to-person transmission[20]. Since then, there was no large single source outbreak and the number of outbreak was decreased. Over the past two years (2003 and 2004), there were only six outbreaks notified, each affecting two persons only. This observation suggested a possible change in the pattern of Hepatitis A outbreaks.

23. As for risk factors, a local study in 1997 found that 57% of the hepatitis A patients had history of shellfish consumption within 6 weeks prior to onset of symptoms[16]. This is consistent with recent data from 2003 to 2004 which showed that 56% (128 cases) of the 227 reported cases had history of consumption of shellfish. However, causality cannot be established in the absence of appropriate control groups as the consumption of shellfish is very popular in Hong Kong. A local food consumption study among general public conducted in 2000 revealed that 61.1% of respondents had history of consuming shellfish in the month before enumeration[17]. Moreover, the long incubation period of hepatitis A introduces uncertainties during the

investigation of sporadic cases in establishing causal relationship with any specific food vehicle. Any remnant of the implicated food is usually not available for testing by the time the disease is manifested clinically. Regarding other risk factors reported in overseas studies such as sexual contact, injection-drug use and attending care facilities, further local studies would be required in view of lack of local data in this regard.

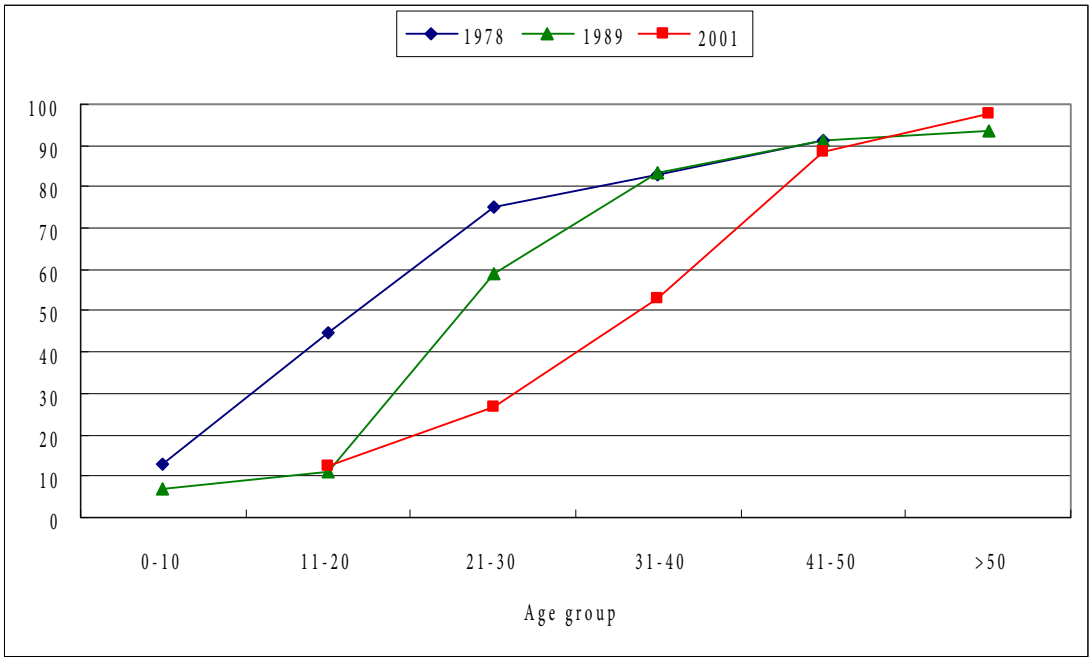
Mortality and morbidity

24. Overall case fatality rates had been low and ranged between 0 and 0.9% (1 to 4 cases per year) for the period from 1988 to 2004. Among the 227 cases reported in 2003 and 2004, 58.6% required hospitalization and one had died. The median length of stay was 5 days and the range was 1 to 25 days.

Seroprevalence studies

25. Serological surveillance studies showed a general decrease in overall prevalence of anti-HAV over the past 2 decades with a right-shifting of age-specific seroprevalence (Figure 4). Seroprevalence rate of adult age 21-30 has been decreased from 75.0% in 1978 to 26.8% in 2001[18]. A study in 1999 found that the overall prevalence of anti-HAV among secondary school students was 7% and the seroprevalence increases with age. The rates were higher amongst those who were born in the Mainland and those whose parents were with lower educational level and engaged in less skilled occupations[19,20].

Figure 4 Sero-prevalance of Hepatitis A in different age groups in 1978, 1989 and 2001[18,21]



Current control measures

26. Worldwide, improved environmental sanitation to prevent faecal contamination of food and water has been the most important means of preventing hepatitis A infection. In the absence of specific treatment, the World Health Organisation (WHO) advocates a preventive approach to hepatitis A encompassing elements of (a) primary prevention and (b) epidemic measures[9].

27. The key components of primary prevention include providing safe drinking water and proper disposal of sanitary waste, monitoring waterbeds where shellfish are harvested, monitoring disease incidence, early detection of outbreaks, and an immunization strategy which is relevant to the local epidemiological situation.

28. On the other hand, epidemic measures refer to outbreak control and the emphasis is on determining sources of infection, identifying contacts of case-patients for post-exposure prophylaxis, and containing disease spread.

29. In the following, we examined the existing control measures focusing on food control, outbreak investigation and control, immunization and public education.

Food control

30. Hepatitis A virus can be present in food and cause large outbreaks[22,23]. Shellfish, especially the bivalves, are considered as high-risk food associated with hepatitis A infections[24,25].

31. In Hong Kong, the Centre of Food Safety (CFS) of the Food and Environmental Hygiene Department (FEHD) is responsible for enforcement of food safety legislation and conducting food surveillance and import control. Under the Public Health and Municipal Services Ordinance, Cap 132, fresh or frozen shellfish is classified as a restricted food item and is subjected to control. At the import level, importers are encouraged to obtain health certificates issued by health authorities of the countries of origin certifying that the consignment is from approved source and fit for consumption. Under the food surveillance programme, FEHD inspects and samples shellfish from the retail/wholesale outlets and at entry points for testing of HAV on a regular basis. The detection rate of hepatitis A under the programme has dropped from 5 to 10% in the last decade, to some 2% in the last 5 years. Moreover, the positive samples identified in the last 5 years were all raw bivalves that were not supposed to be eaten raw.

Outbreak investigation and control

32. 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.

33. 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.

Immunization

34. Both passive and active immunization are effective in the prevention of hepatitis A infection. Passive immunization with immune globulin is effective in providing short term pre-exposure protection (3 to 5 months) and is effective for post-exposure prophylaxis if given within 14 days of exposure. However, it is considered relatively costly compared to active immunization.

35. Several inactivated vaccines are licensed and commercially available for active immunization against hepatitis A. The vaccines are given parenterally as a 2-dose series, 6 to 18 months apart. None of the vaccines are licensed for use in those younger than one year. These vaccines have been demonstrated to be highly immunogenic. Nearly 100% adults will develop protective levels of antibody within one month after a single dose of vaccine. Field studies of protective efficacy have found cumulative rates of 95 to 100%. Kinetic models of antibody decay found that the duration of protection is likely to be at least 20 years, and possibly lifelong[11]. A combined vaccine for hepatitis A and hepatitis B is also available.

36. According to the WHO, the best vaccination strategy for a region should be determined by the epidemiology of HAV, the risk groups, the duration of protection, the possibility of post-exposure protection, and the cost of the intervention. In general, the groups at high risk of HAV infection as a result of behaviour, lifestyle, or occupation should be the primary target for a hepatitis A vaccination programme[9]. Countries like the USA, Canada, and Australia have set out their vaccination strategies addressing the special needs of (i) those living in localized areas of high disease activity, (ii) those who are at increased risk of exposure, (iii) those with chronic liver disease, (iv) outbreak situations.

37. In Hong Kong, the former Scientific Working Group on Viral Hepatitis Prevention considered in 1997 that the role of mass immunization for hepatitis A immunization remained to be demonstrated and recommended that hepatitis A vaccination strategy be reviewed from time to time in line with international and local developments. The Scientific Committee on Vaccine Preventable Disease also recommended the same position. It also recommended the following groups to have hepatitis A vaccination for personal protection: (a) Persons with chronic liver disease; (b) Persons with clotting factors disorders receiving plasma-derived replacement clotting factors; and (c) Travelers to endemic areas. Regarding the remaining groups which have good overseas evidence for higher infection risk, local studies are called to better characterize the recommendation for hepatitis A vaccination in view of lack of local substantive data. Post-exposure prophylaxis (vaccination and immunoglobulin) may be considered for control of hepatitis A outbreaks occurring in closed institution yet routine use for contacts of sporadic case is not recommended.

Public education

38. Both DH and FEHD contribute to public education on the prevention of foodborne infections. Since hepatitis A infection is transmitted through the fecal-oral route, promoting good personal and food hygiene is of importance in preventing infection. Health advice is delivered to the public through health talks, health educational pamphlets, and the media.

Changing epidemiology and its implications

39. With development of advanced water systems and sanitary conditions over the past few decades, Hong Kong has moved from being a hepatitis A endemic area to an area of intermediate endemicity. Recent data suggested that we might be in transition from an area of intermediate endemicity to low endemicity. The previous analysis showed that Hong Kong has a declining incidence of hepatitis A over the past 2 decades and there was an increase in the age of the reported cases. There was also right-shifting of the seroprevalence rates across the age cohorts. The proportion of those susceptible to hepatitis A infection is likely to increase further in the coming decades. Lowering of overall herd immunity would lead to higher risk of outbreaks once the pathogen is introduced into the community.

40. Although disease incidence remains low, the gradual accumulation of adults susceptible to hepatitis A infection in the population (who are prone to more severe illness) calls for a shift in our emphasis towards enhancing measures for case detection and early prevention of outbreaks and their associated morbidity. It is therefore necessary to re-examine our current strategies.

Recommendations

Enhancing disease investigation and outbreak detection

41. 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.

42. During community outbreaks, demonstration of the presence of HAV in stool or serum using reverse transcriptase-PCR technique coupled with fingerprinting of virus by nucleotide sequence analysis can help differentiate the genotypes and determine clustering of related cases, which could ultimately enable tracing of the origin of infection[26,27]. Comparison with the virus circulating in the region can also distinguish between local and imported sources[28]. For early identification of outbreaks and facilitation of source identification, we recommend that laboratory support be strengthened to include molecular studies for hepatitis A.

Conducting systematic seroprevalance studies

43. In view of the right-shifting of seroprevalence rates demonstrated by adhoc studies, there is a need to better monitor the epidemiological situation of hepatitis A through regular surveys. To this end, we recommend that serial cross-sectional serological surveys using similar sampling methodologies covering different age groups be conducted every 5 to 10 years to guide public health actions on hepatitis A prevention.

Protecting people against food –borne Hepatitis A infection*s*

44. Foodborne HAV transmission still carries the greatest risk of large scale outbreaks. Under the food surveillance programme, CFS regularly inspects and samples shellfish from the retail/wholesale outlets and at entry points for testing of HAV. However, prior approval from CFS was not required for import of seafood including shellfish. To prevent food-borne transmission of hepatitis A, we recommend that existing food safety legislations on imported seafood especially shellfish should be reviewed, taking reference from international practices and guidelines. The current food surveillance programme should also be continued with wide dissemination of results through various means to alert the public of the risks of consuming various foods and advice on the specific food hygiene measures for preventing the disease. Alertness to foodborne hepatitis A outbreaks in countries which may import food to Hong Kong should be maintained.

Reviewing vaccination strategies

45. In view of the latest epidemiology of hepatitis A in Hong Kong and the international practice, hepatitis A vaccination is recommendation for the following groups for personal protection: (a) Persons with chronic liver disease; (b) Persons with clotting factors disorders receiving plasma-derived replacement clotting factors; and (c) Travelers to endemic areas. Regarding the other groups which have good overseas evidence for higher infection risk, local studies are called to better characterize the recommendation for hepatitis A vaccination in view of lack of local substantive data. Post-exposure prophylaxis (vaccination and immunoglobulin) may be considered for control of hepatitis A outbreaks occurring in closed institutions. As for post-exposure prophylaxis for contacts of sporadic cases, the value of routine use in local setting as a public health measure is not proven but may be recommended on the ground of personal protection.

Strengthen public awareness

46. To enhance public awareness on food hygiene, we recommend that education programmes be conducted regularly through various channels, aiming at modifiying high risk consumption behaviours. Training for food handlers should also be provided to ensure adequate knowledge on the proper food handling practices. The public should be warned of the risk of consuming raw or undercooked shellfish. Health advice should be both specific and practical and should include details on minimum cooking time for HAV inactivation. Effort must be made to ensure health messages are accurate and clear. For instance, although the public was generally advised to soak shellfish in clean water for half a day for removing dirt and impurities[17], such action should not be confused with commercially performed depuration. Depuration is a controlled process undertaken by depuration plants. It relies on the ability of shellfish to purge their gastrointestinal contents by filtering clean seawater[29]. Performed under the right conditions and duration, which may vary from 1 to 7 days, it is an effective process for elimination of faecal bacteria but not enteric viruses[30].

Summary of recommendations

47. The recommended public health strategies for prevention of hepatitis A in Hong Kong are summarized as follows:

1. Enhancing disease investigation and outbreak detection
   - To maintain the capacity to perform molecular characterization and to apply these techniques for hepatitis A surveillance and early detection of outbreaks
2. Monitoring seroepidemiology
   - To conduct regular serological surveys on hepatitis A for

monitoring of the changes in epidemiology

3. Preventing foodborne HAV infection
   - To review existing food safety legislation on imported seafood, with reference to international practices and developments
   - To maintain regular surveillance of hepatitis A in food samples
4. Reviewing vaccination strategies
   - To review and recommend on a hepatitis A vaccination strategy based on current epidemiology
5. Strengthening public education
   - To publicise risks of hepatitis A through various channels and raise awareness on food hygiene and the proper preventive measures
   - To ensure adequate training for food handlers

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Appendix 1

Prevalence of anti-HAV in a collection of studies/testings between 1978 and 2003 (data sources: multiple sources)

[directly extracted from ref. 18]

Age group	1978	1987	1989	1993	1995	1996		1998	2000	2001	2001	2002	2003
0-10	12.9	5.3	6.8	59.8(M) 53.5(F)	8.3		6.1	5.4	9.3	4.58		5.3	10.3
11-20	44.8	17.1	11.2			7.0					12.5		
21-30	75.0	53.8	58.8		11.3		11.8	7.6	17.5	13.2	26.8	12.6	13.2
31-40	82.9	85.1	83.5		49.0		37.7	40.8	35.0	41.3	53.2	46.7	52.4
41-50	91.1	94.7	91.1	94.5(M) 91.0(F)	70.5		58.6	66.7	60.0	71.1	88.3	58.1	100.0
>50			93.9								97.7		
Data source	A	B	C	D	E	F	E	E	E	E	G	E	E

Data sources:

A. Study on left-over sera of 362 subjects, by Tsang et al of University of Hong Kong
B. Study on stored sera of 702 healthy subjects, by Chin et al of University of Hong Kong.
C. Study on 1028 serum samples collected from individuals attending a health exhibition, by Lim et al of Department of Health.
D. Seroprevalence results reported in the press by Lai et al of University of Hong Kong.
E. Pre-vaccination screening on students and staff of City University of Hong Kong: 553 (1995), 669 (1996), 608 (1998), 395 (2000), 592 (2001), 372 (2002) and students and staff of Baptist University of Hong Kong 240 (2001), 259 (2002), 153 (2003) and students and staff of Lingnan University 125 (2003).
F. Seroprevalence study in school children by Lee et al of the Chinese University of Hong Kong.
G. Community Research Project on Viral Hepatitis 2001.

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